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ORGAN OF THE AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE AND THE JOHNS HOPKINS INSTITUTE OF THE HISTORY OF MEDICINE

Editor—HENRY E. SIGERIST

Associate Editor—GENEVIEVE MILLER

VOLUME XVI NOVEMBER, 1944 NUMBER 4

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THE HEROIC AGE OF GERMAN MEDICINE*

ADOLF MAGNUS-LEVY

"Wohl dem, der seiner Väter gern gedenkt"

The second half of the nineteenth century was the heroic age of German medicine, and of the other sciences as well. The author of this paper had the good fortune to grow up in Germany during this Epoch. It was also the golden age of the universities. The poets sang, "von Deutschlands hohen Schulen." None of the universities fell below a dignified standard. Even where a small provincial university as a whole made less appeal to students and teachers, yet in one or the other of its departments it usually proved to have strong magnetic power. Only once perhaps at that time, between 1873 and 1890, one place outshone all the others because of the uniformly high standard of all its faculties, the University of Strassburg. When this university was reestablished in 1871, the most outstanding professors at the peak of activity in their respective fields were called from the whole German Empire. The watchword of the time was

*From the Historical Library, Yale University School of Medicine, New Haven, Connecticut. The research was undertaken with the assistance of a grant from the Dazian Foundation.

These random memories of the German universities and their teachers were intended originally as an appendix to a survey of the development of metabolic science in Germany. Only at the suggestion of interested friends is it published here. For the English form of this paper the author is under obligation to Dr. F. W. Lenz and Prof. G. L. Hendrickson.

" science without prejudice and without preconception " (voraussetzungslose Wissenschaft), to use a term employed by Theodor Mommsen, so far as such objectivity is possible. Side by side with this conception was the idea of " academic freedom," and unrestricted liberty of movement from one university to another, which proved to be of great value both to professors and students. The great majority of the professors changed the places of their activity several times in their career from docent to assistant professor and full professor, and even full professors seldom remained permanently in the chairs to which they were first called. The ambition for a better and wider sphere of activity kept their passion for work alive; a new call compelled them to face new tasks, to adapt themselves to a new environment, and inspired them in many ways through contact with their new colleagues in their own field and in related departments.

In his instruction the full professor covered the essential content of his special field in five to eight lectures each week. This task made it necessary for him to master the entire subject, to grasp it as a whole, yet with freedom to present it in his own way. Where the professor combined distinguished scholarship and research with skill as a teacher, he made a deep and lasting impression on his students.

From time to time some teachers of special distinction presented public lectures once or twice a week which were open to students of all faculties. Such semi-public lectures enjoyed great popularity, and it might well happen that the student, eager to hear Treitschke, the historian, or Mendel the neurologist, would be turned back from the closed doors of the over-crowded auditorium maximum. Similar opportunities were afforded on occasions of academic festivals, the inauguration of the Rector Magnificus, the commemoration of some great figure of the past. The effect was heightened by the free, animated delivery of such lectures, no manuscript, no reading,—a usage which extended to less formal occasions of medical societies and congresses.

At that time the student entered the university at eighteen to twenty years of age, after a preparation which was quite different from that customary in the English speaking countries. The preparatory training was usually obtained in one school, which up to the end of the nineteenth century was the classical Gymnasium, with its systematic training in Latin and Greek. This was the recognized place of preparation for students with higher aspirations. They attended it, if it had also the elementary or pre-high school grades, from the seventh up to the eighteenth or twentieth year. At that time in England also and in America classical

training was in the foreground for the more ambitious students of the higher and middle classes. Even today many leaders in German science were prepared in the classical Gymnasium. It cannot however be denied that, in consequence of the great enlargement of educated circles and the ever increasing influence of science and technology, this type of school has lost much of its former importance.

A peculiarity of German university training and of its "academic freedom" was the lack of continuous control of the work and attainments of students by annual or semi-annual examinations. It is needless to say, however, that evidence of adequate mastery of the subjects prescribed was required of every one. At that time, the student of medicine took the first medical examination, the so-called "tentamen physicum," which included natural sciences, anatomy, and physiology, after four semesters (two years). The examination for the doctor's degree and the state examination, the most important of all, followed after four or five more semesters. Later the duration of study was somewhat extended. With very few exceptions, the examinations were oral and offered to the candidate the opportunity to show not only what he had learned but also how far he had understood and assimilated his learning. If the examiner was discerning and considerate—not all of them were—it happened sometimes that, in spite of one or two serious blunders at the beginning of the examination, a candidate was able to correct himself and to reveal a real knowledge of facts and their relations, so that, to his own surprise, he finally emerged with a "summa cum laude." Confidence in the diligence and self-discipline of the students generally proved to be well founded, and the freedom granted them favored the development of individuality, and contributed to producing original investigators and teachers.

Some well-known exaggerations of academic freedom, such as "Saufen und Raufen" (drinking and duelling), were generally limited to smaller circles and to the earlier semesters, after which students quickly came to their senses and went to work. Even the members of the aristocratic student clubs, with their colored caps and regalia, proved eventually not so indifferent to serious life as they seemed.

Usually the student attended more than one university, unless external circumstances, in most cases financial, prevented him. He changed his university two and three times, sometimes even more frequently. The student whose home was somewhere in North Germany found it pleasant to enjoy a semester among the natural beauties of the South and the gayer temperament of its people. Heidelberg and Freiburg invited him in summer, Munich in winter. Much more important however for the

choice of a university was its significancy as a seat of learning and the attraction of its staff of teachers. In this way the wandering scholar, our "Bruder Studio," became acquainted with many great names in his own field, and occasionally also with the greatest representatives of other sciences. These changes prevented him from onesidedness and partial judgments and from limiting himself too much to his special department of study. Especially in the smaller universities was it possible and easy to make friendships with students of widely different interests from his own, and to find in them congenial and stimulating comradeship.

The privileges and advantages of that time of academic freedom of study and of migration from one seat of learning to another the present writer had the good fortune to enjoy to the full. His nine years of study of medicine, of chemistry and related subjects led him to two universities in North Germany, Berlin and Leipzig, and to three universities of the South, Heidelberg, Tübingen and Freiburg. For eight following years he had the opportunity to work as a clinical assistant in Berlin, Frankfort, and Strassburg. In addition, on occasional and mostly short visits, he became acquainted with all the German universities except one. In this way he felt the influence of many important teachers. To fix and to preserve some characteristic features of their personalities is the purpose of the following pages. "Thou owest greater thanks to thy teachers than to thy father: for he gave thee only bodily existence, but they gave thee thy spiritual life." [1]

Bunsen, professor in the University of Heidelberg, the greatest inorganic chemist of his time, tall of stature and of imposing physique, still at the age of seventy-three attracted throngs of students by his spirited lectures, his skillful experiments, and by the warmth of his personality. He and the philosopher Kuno Fischer were the first scholars to receive from a magnanimous Regent the title of "Excellenz," who thereby paid homage to science. This example was followed by others, but fortunately not too often. When this honor was bestowed upon scholars such as Koch and Ehrlich, or the physicist Planck and Harnack, professor of church history, there was every reason for being pleased with such recognition.[2] In the democratic monarchy of Great Britain too, pre-eminent scholars and leaders in science have been honored by knighthood or baronetcy. To show himself too eager for this honor was wisely esteemed good ground for letting the aspirant wait a long time. Theodor Mommsen declined it altogether.

[1] From the "proverbs of the Fathers," about 100 B. C.

[2] The courts of Munich and Vienna bestowed personal nobility on outstanding scholars.

A. W. Hofmann, founder of the science and industry of dye stuffs, was active in earlier years in England for about a decade. At the age of 40, although a foreigner, he became president of the Royal Society of Chemistry. His vigor and animation even in advanced age, the freshness of his countenance with his sparkling blue eyes, set in a frame of white hair, left an abiding picture upon the memory of his auditors, along with the content of his discourse.

Helmholtz was the greatest German scientist of the century. Unfortunately however he was not a good lecturer, at least not for elementary physics. When he was appointed head of the Reichs-Institute of Physics, his successor was Kundt, an excellent teacher, with whom the author of this paper was able to make up the defects of earlier study in this field.

Gegenbaur was the first to base anatomical instruction on comparative anatomy. He was however not able to inspire his students with interest in the rather arid subjects of osteology and syndesmology.

Waldeyer, founder of the doctrine of neurons, was a superb organizer. At that time, when there were only a few large size anatomical charts and no lantern projections, he was able with marvellous skill to present on the blackboard with crayons of different colors the shape, position, and relations of organs—all done with rapid free hand drawing, whether to scale or in natural size. From his course on descriptive anatomy, which he gave for seven or eight hours a week before a class of three or four hundred, there were seldom absentees. His courses of dissection were attended by as many as six or seven hundred students. Every day of the week, during two winter semesters, the student of medicine had to work for several hours daily in the hall of dissection. The enormous task of supervising the work of such a number of students he performed brilliantly with the help of a staff of twenty or thirty assistants. There was at that time, even in Berlin, no system of refrigeration. Carbolic acid was, therefore, used in very large quantities, and there was throughout the whole building its characteristic and penetrating smell. Even so it was impossible to protect the cadavers from putrescence and lividity. The knowledge of the topographical relations of the organs was completed in the more advanced stages of study by observations on the living body under the direction of surgeons.

In Berlin Du Bois-Reymond, a descendant of one of the old Huguenot families, taught physiology. He had at that time, one may say with all charity, outlived himself. His lectures which had not for many years been revised and renewed were disappointing. The eloquence and moving power of this great and talented man had lost much of its original warmth

and freshness. At the pinnacle of his fame he had concluded a discourse on "The limits of our knowledge of nature" with the austere word "ignorabimus" (we shall never know). It was a renunciation and a challenge to the dull and barren materialism which, after 1850, had been propounded by Moleschott and Büchner (in his "Kraft und Stoff"). This warning was greatly appreciated by every philosophical thinker. Although it was not meant as renunciation of investigation and of progress, yet its sound was disconsolate and depressing. It is not "ignorabimus" that is written on the walls of the auditorium in the Harnack-Hall in Dahlem, where the leaders of the sciences hold their meetings, but the words of a deeper genius, Goethe, the student of nature, which reads as follows: "Das höchste Glück des denkenden Menschen ist es, das Erforschliche erforscht zu haben und das Unerforschliche ruhig zu verehren." [3]

Carl Ludwig, along with Helmholtz and Virchow, the most outstanding figure in medicine of his generation, remained vigorous and active well into the seventies. The author of this paper attended Ludwig's lectures in the third and fourth years of his study for a second time. Ludwig's influence was so decisive as to cause him to continue the study of medicine, which he had planned to abandon in favor of history, although he had at that time reached the advanced clinical semesters. "Ludwig's papers were epoch making; he was the greatest teacher of his subject who ever lived, and founder of the largest school of physiologists." "A quiet, noble, distinguished gentleman, always well dressed though old-fashioned, he ranked as one of the finest types produced by our civilization." (The judgments of an Englishman and an American.) When in a darkened room the dim light fell on his face and the animal he was handling, he resembled a wizard of olden times. Ludwig compared the very inadequate methods of that time, of cutting and removing parts for the purpose of studying the functions of the nervous system, to an attempt to explore the mechanism of a clock by pistol-shots. He was not devoid of sarcasm. Once when during an experiment a decapitated frog jumped from the desk and the students began to laugh, Ludwig rebuking them said in his quiet and dignified manner: "You see, young gentlemen, how little brain is needed in order to provoke laughter from a student's brain."

Ernst Wagner had taught pathological anatomy at the University of Leipzig for twenty years before he received the chair of internal medicine. In both fields he was an able and earnest teacher. At that time such a

[3] "It is the supreme good of thinking man to seek and to find that which can be found, and to contemplate with quiet reverence that which lies beyond human inquiry.

change of subject, not unusual in previous periods, took place rarely. In like manner, twenty years before, Frerichs became the most distinguished internal clinician of his time after changing, " with great reluctance and almost with aversion," from chemistry and physiology to the clinic.

W. Erb at Heidelberg had a preeminent share in developing neurology. The symptoms of the nervous affections had to be determined, the different diseases to be formed into groups, and their aetiology to be established. That was the task of those years. Erb in this respect did much for the diseases of the spinal marrow, for the dystrophia musculorum and for the claudicatio intermittens (intermittent limping). His most important contribution was the establishment of the syphilitic aetiology of the tabes dorsalis, which he did almost simultaneously with Fournier of Paris. Both of them inferred the postsyphilic nature of that dread disease from the anamnesis of their patients.[4] Later on E. Mendel did the same for dementia paralytica. Wassermann and Noguchi led this doctrine to victory by introducing complement fixation, and by demonstrating the existence of spirochete in the brains of paralytics. Erb, very impressive with his robust Palatinate dialect and nature, was fond of illustrating before his students with his own arms and legs the various disturbances of motion in his patients. His teaching of internal medicine proper was in no way inferior to his treatment of neurology.

In surgery asepsis was introduced after 1880 and used at first along with antisepsis, but replaced it later on completely. It made possible the first successful operations on the brain, a department of surgery which Czerny of Heidelberg took over with great zeal and success. Thiersch of Leipzig was opposed to the admission of women who began at that time to attend the universities. His biting wit did not spare women themselves nor even members of the royal house.

At that time pharmacology and hygiene were at first represented only in a few larger cities by research scholars who had grown up in these fields. At smaller universities, for instance at Heidelberg, the instruction in pharmacology and exercises in making up prescriptions were still in the hands of experienced practitioners who had familiarized themselves with the new demands of the time. It was scarcely first hand instruction.

Somewhat better was the situation in the field of pediatrics, although it took decades and many difficulties had to be surmounted before it was recognized as an independent department and special chairs were estab-

[4] From inferring the presence of earlier luetic infection, with certainty in 30% of cases and with probability in 20%, he became able by degrees to increase this proportion to 60% and 30% respectively.

lished. Consequently pediatrics, although taught by experienced physicians, was regarded merely as one department of general internal medicine. The foundations of modern pediatrics as an independent science were laid by a later generation of scholars such as Heubner and Czerny.

The then young doctor who writes these reminiscences was advised by the aged professor Ludwig to become acquainted with N. Zuntz in Berlin, and to acquire from him a good physiological training. Zuntz entrusted him with a large problem of research on gaseous metabolism. This investigation gave occasion to introduce to clinical use the respiratory apparatus of Zuntz-Geppert, of which little use had been made up to that time, and to establish the main function of the thyroid gland. This modest but able and penetrating scientist, teaching in an agricultural institute, became of service to practitioners and to investigators as well. He was fertile in suggesting themes for younger workers, and was much in demand as a contributor to the programmes of various medical societies.

Among the outstanding physiological chemists, the author of this paper had the opportunity to work during many years with Drechsel and Baumann, with Franz Hofmeister and Salkowski. He became well acquainted also with Kühne and Jaffe, Hoppe-Seyler and Schmiedeberg.

Albert Fraenkel, from the school of Ludwig Traube, was a master of the old " classical " diagnostics of diseases of the heart and the lungs. To his helpers and assistants he was a great teacher. His head, like the heads of so many others—fortunately only the head of his bust which stood at the entrance to the hospital—fell a victim to the fury of the Nazi iconoclasts in 1933. He was best known for his discovery of the pneumococcus. Since Virchow, because of his one-sided morphological point of view, was opposed to bacteriology, it was necessary for Fraenkel to take the material for his research by stealth from the celler in which the cadavers were kept.

The strongest and most powerful influence was exerted on the present writer by Bernhard Naunyn (1839-1925), whose assistant he became at the end of his years of apprenticeship. It was not so much that Naunyn determined the general direction of the author's research, or suggested to him problems of investigation; it was rather Naunyn's lofty spirit and breadth of vision which influenced him. Above scientific achievement stands personality.[5] " Naunyn, der ist ein grande " were the words with which Fr. Müller once declined to compare the clinician of Strassburg

[5] It is needless to remind my American friends of men of similar type, such as Osler and Welch, whose influence was however more widely felt because they worked in a field which had been less widely cultivated up to that time.

with any of his colleagues. During the first half of his activity Naunyn was esteemed chiefly as an experimental pathologist; only later in his career was it recognized that "the blood of a clinician was in his veins." His book on diabetes still remains the most mature work that has ever been written on this disease, although the data which he presented soon, and by degrees also his general point of view, was surpassed. The physicist W. Nernst characterized Naunyn's autobiography as the most important work of its kind ever written by a physician. It bears the title "Reminiscences, thoughts and opinions." The significance of these Reminiscences lies in his sharp and penetrating reaction to the significant circumstances of his personal life and professional experience, and no less in his brief and lucid expression of it. Unfortunately his non-technical papers, not many in number and none of them long, were reprinted only in a private edition of one hundred copies of his *Gesammelte Abhandlungen*. They include besides a series of tributes in memory of important fellow workers in medicine, a survey of the development of internal medicine (Die Berliner Schule), a discussion of the physician's calling, its difficulties and tragedies (Aerzte und Laien), and similar subjects. His dictum, "Die Medizin wird Wissenschaft sein, oder sie wird nicht sein," gave rise to lively debate.[6] The significance of this utterance and the range of its validity will not be disputed by any serious and thoughtful physician. It will be surprising however to American doctors, although they too know in their own country cross currents and under currents of a turbid kind, that, since 1900 and particularly in the period of decline after 1918, large circles of doctors were opposed to so rigorous a standard. Among them are to be found not only representatives of so-called "natural medicine" and advanced modern homeopathy, but also surgeons of rank who starting from the "technique" of their limited field aimed at general therapeutics, but even a considerable number of regular practitioners. They regarded Naunyn's standpoint as a misconception and inadequate appreciation of their personal share in practical medicine, of their ability and of their "art." It remains true that every good physician must have this personal skill or art, just as it is equally true that great research scholars without vision or intuition are unthinkable. "Progress as a whole, however, is based on science, not on medicine as art!" "Nothing protects the man more against giving up the solid ground of what is accessible for what is inaccessible, and against exhausting himself in futile

[6] In less epigrammatic form: "Nur in der Wissenschaft liegt das Heil der Medizin"—words which he used in his Dorpat inaugural lecture and called his confession of faith. Cf. *Erinnerungen*, p. 190.

dreams and phantasmagoria, than a solid foundation of scientific knowledge." Naunyn's conception of the imperative place of science in medicine, and his attitude to the human ethics and tragedy in the profession of a physician, made him the exponent of the medical conscience of his time.

It was not until he had passed his student years that the present writer became acquainted with the leading medical authorities of Berlin; some of them, like Leyden and Gerhardt, as presiding officers of medical societies or clubs. In Berlin there were almost too many specialists and their clubs. The "Medical Society" was the chief centre of interest. Its focus was Virchow, one of its founders. The veneration felt for his preeminence was associated with diffidence toward him and even with a certain fear. He ruled the Society with absolute authority in all its affairs, and not always to its advantage and convenience, a trait characteristic of his bearing elsewhere as well. The surgeon E. von Bergmann succeeded him—like Virchow, authoritative, sovereign, but of a temperament not always happy nor just. After two other more objective and less colorful presidents, Senator and Orth, to the surprise of all Fr. Kraus proved to be the best president of all. Since his coming to Berlin he had earned an unfortunate reputation, both in his lectures and in his clinical work, for quite irrelevant and inept "eloquence." Here on the contrary, as presiding officer of so large an organization, he displayed extreme lucidity and concentration in conducting the debates, as well as good judgment in selecting appropriate and interesting subjects for lectures and discussions. In addition to these merits he had a full understanding of professional needs and the social-ethical difficulties of the profession, in particular for those of the "insurance doctors" (the Kassenaerzte), whose practice was confined to the humble contributors to social security funds.

Among the clinicians of his generation the author had close relations with O. Minkowski and Fr. Müller, with W. His, von Mering, Ad. Czerny and others. Minkowski, the "ambidextrous," was the first successfully to remove the liver and the pancreas, the latter at the very first attempt: the first dog operated upon survived longest of all! The discovery of insulin filled him with joy and with admiration for the discoverer. The great tradition of the Berlin school, which in Frerichs, Naunyn, and Minkowski, had in three generations produced three successful investigators in the same field, was continued on a modest scale by the assistants of Minkowski, investigating the working of insulin. Although Minkowski showed not the slightest interest in practical surgery, yet his skill was such that after a short preparatory training of the patient he

was able to remove a polypus from the anterior commissure of the larynx. No one of the competent surgeons who had been called previously had ventured to risk this operation. His marvellous keenness of intelelct enabled him to meet in successful debate opponents even in other branches of inquiry, and on their own ground to put them to rout.

Fr. Müller was an excellent and indefatigable synthesist. He stood "mit markigen Knochen auf der festgegründeten Erde." He knew how to make the right use of every detail, even if it was only the mortar to bind together the stones for his edifice. His constructive method pleased greatly the American colleagues before whom he delivered many lectures. His manual of medical-clinical diagnosis went through forty-eight editions in fifty years, and deserved this popularity. Every new edition showed traces of careful revision with reference to the most recent discoveries. Although under compulsory retirement at the age of seventy-two, he still had for several years the satisfaction of seeing three hundred or more students facing him three times a week. With Wilhelm His, the discoverer of the "bundle," the author enjoyed a belated friendship when both were past sixty. His was no indefatigable worker; the "demon of work" did not drive him on. In excuse and justification he said: "If I had had the talent to do things like Behring or Ehrlich, it would have been worthwhile to work hard." He was a man of spirit and culture, at home in many fields, and finding in them discriminating enjoyment. It is an interesting and characteristic fact that he published the discovery of the "bundle" with very brief and objective description. It was not until thirty years afterward that he told how he came upon it. His name has become associated with an anatomical substratum, the "bundle of His"; anatomical terms are not subject to the changes of time. Von Mering was another character not greatly devoted to hard work. "I work only when an idea occurs to me," he used to say. Fortunately however ideas were not unusual with him. But most of the German clinicians were diligent workers, as was their duty and their taste as well. With Czerny, who worked at the Charité at the same time, the author became associated by reason of similar lines of work leading to frequent exchange of ideas and opinions. A considerable difference in the age of our patients proved no barrier; there are no essential differences between the metabolism of adults and children.

Of the German medical profession as a whole and of its outstanding figures it may be said to their credit, that in spite of diligent devotion to their calling they were not completely absorbed in it. More than other professional circles, as the jurists for example, they retained an interest

in historical and philosophical studies, in literature, and the familiar ancient classics of their school days. This was true even of the much harassed insurance doctors. One of them, for instance, whose activity lay in the slums of Berlin, was a real connoisseur of Goethe. Most widely diffused was the interest in music. In Berlin there were two orchestras whose members were doctors exclusively. His and Czerny were violinists of first rank; others conducted small private orchestras. The performances of the classical Joachim quartet were never missed by Helmholtz and other famous scientists. Many physicians were to be found at the lectures of wider appeal which were offered by the Academy of Science.

The general habit of life of German and other European doctors and scholars was different from that which is usual in the New World. Uninterrupted work, which is the usual thing here, and which does not admit of intermission and relaxation, was unknown in Europe. Even physicians of modest practice and income usually granted themselves an annual vacation of several weeks for refreshment in the open. Successful and hard driven specialists would take brief outings even more often. Was that only the symptom of a tired culture which had grown old? Was it not rather a legitimate pursuit of happiness to which even the physician had a just claim? Happiness which is not limited to the consciousness of doing his duty and of performing the chosen work; but a happiness only to be found in rest, in "vacation from Self," in a brief return to Nature. Like the interruption of our daily work by sleep, so such an intermission of effort means a "creative pause," as a German philosopher has happily called it.

The heroic age of German medicine came to an end. No golden age in any field and in any nation lasts longer than one or two generations. In the earlier years of the twentieth century German medicine still administered worthily a rich heritage. Then the crime of 1933 put an ignominious end to a great tradition and blighted a prolific growth. In the soil thus blasted let us hope that some living roots still survive to yield with time a new growth.

HISTORICAL NOTE ON THE *NOEUD VITAL* OR RESPIRATORY CENTER

J. M. D. OLMSTED

The 8th edition of the Dictionary of the French Academy gives two meanings for the expression *noeud vital*: the first is its use in physiology to designate "the point in the *medulla oblongata* which governs all the respiratory movements of an animal, lesion of which suffices to kill the animal immediately"; the second is its use in botany to designate "the median line which lies at the collar of a plant between its roots and branches." The Academicians may perhaps be justified in placing the physiological use of the term first on the ground of its importance in present-day medical science, but historically the botanical meaning came first and the term was borrowed for use in animal physiology.

The striking difference between the root and stem of the common plant must have been a very early observation, and the reason why the root should descend into the earth and the stem rise into the air became a matter of philosophical speculation. Experiment seemed to justify the view that the life of the plant must reside in its "collar," i. e. that region where root and stem have their common origin, since if one cuts off the parts above this level, the severed stem will die and a new stem may grow up from the collar; or if one cuts off the parts below this level, the severed root will die and a new one may grow down from the collar. So important did this part of the plant appear to Cesalpino (1519-1603), whose botany is permeated with Aristotelian philosophy, that he located here the soul of the plant—a nutritive soul only, to be sure, since he agreed with Aristotle that plants are neither sensitive nor motile, and therefore lack an *anima sensitiva motivaque*.[1] Lamarck (1744-1829) in his *Histoire naturelle des végétaux*[2] which he published in 1802 with Mirbel as co-author, elaborated further this ancient idea of the importance to the plant of its collar, pointing out that it serves as the necessary link between the root, the organ which extracts nutritive material from the soil for the whole plant, and the stem, the organ which bears the generative organs. To emphasize the relationship he applied to this essential plant structure the expressive term *noeud vital*, which may be translated vital knot, or vital node. He seems to have been proud of the descriptive

[1] Reed, H. S. *A short history of the plant sciences*, Waltham, Mass., 1942, p. 72.
[2] P. 225 *et seq.*

phrase he had made, since in his later writings he was careful to give an exact page reference to his first use of it and to state that the terminology was his own.[3]

The use of *noeud vital* in animal physiology began with Flourens (1794-1867). Flourens always claimed [4] that his first memoir on this subject was read before the Paris Academy of Sciences, December 3, 1827. There is no mention of such an event in the minutes of that date. He did, however, present to the Academy on March 3, 1828 a copy of a memoir entitled, " Nouvelles expériences sur le système nerveux " which had been published in the January (1828) number of the *Annales des sciences naturelles*,[5] and which he later used with only minor changes in wording for the section on the *medulla oblongata* in the second edition of his *Recherches expérimentales*. In the last paragraph of this memoir where he sums up his conception of the functions of this part of the brain, we find him comparing the medulla of vertebrate animals to the collar of plants, and here is the acknowledgment of his indebtedness to Lamarck for the " happy " expression *noeud vital*. This was over a quarter of a century after Lamarck had published his botanical treatise.

It was the observation that injury to a certain very circumscribed area of the medulla results in instant death that led Flourens to borrow the expression. This spot bears an analogy to the botanical *noeud vital* not only because of its situation—it lies between the spinal cord, which is comparable to the root of a plant, and the anterior parts of the central nervous system, viz. cerebral hemispheres, cerebellum and brain stem, which without too great stretch of the imagination may be compared to the parts of a plant above ground—but because it, too, seems to be the seat of life. Cutting off parts of the brain above or below it causes the detached parts to die, but still leaves the urge to breathe, and breath from time immemorial has been the sign of life. Flourens also pointed out that this region serves as an essential link between the reception of stimuli by the lower part of the body and their conscious perception in the brain, and between the will and the means of carrying out the mandates of the will, just as the collar of the plant serves as an intermediary between root and stem.

Flourens was not the first to observe that injury to this particular

[3] Cf. *Philosophie zoologique* (nouvelle edit.), Paris, 1873, v. 1, p. 376.

[4] Cf. *Recherches expérimentales sur les propriétés et les fonctions du système nerveux dans les animaux vertébrés*, Paris, 1842, p. 186; also, *C. R. Acad. Sci.*, Paris, 1851, *33*: 437, and *ibid.*, 1858, *47*: 803.

[5] *Ann. des Sci. Nat.*, 1828, *13*: 86.

region may cause instant death. Homer [6] recorded an illustrative case in a passage which Pope picturesquely translated thus:

> Full headlong from the roof the sleeper fell,
> And snapped the spinal joint, and waked in hell.

Galen actually performed some animal experiments along this line and showed that a transverse section of the spinal cord between the first and second cervical vertebrae will result in cessation of respiratory movements—and death.[7] Although Legallois (1770-1814) is usually credited with the first successful attempt to locate the respiratory center, the earlier work of Lorry (1726-1783) should not be forgotten, in spite of its being only a slight advance over Galen.

In two long memoirs [8] on movements of the brain read before the Paris Academy of Sciences in 1760 Lorry gave his evidence for believing that although neither the brain nor the dura mater can of themselves move, nevertheless the brain is the source of all bodily movement. Three divisions of the brain were recognized at that time, cerebrum, cerebellum, and medulla; the cerebrum was thought to be the seat of animal functions, the cerebellum of vital functions; the medulla being little more than a prolongation of the spinal cord. Therefore injury to or removal of the cerebellum should abolish life. But Lorry found that this was not true. A dog could live for at least a quarter of an hour after removal of the cerebellum and yet show regular respiration and pulse. The same was true after removal of the cerebrum. Severing the spinal cord merely produced paralysis in the regions below the lesion. Lorry therefore concluded that, contrary to prevailing opinion, the medulla must be the seat of all vital and animal movement. He then attempted to locate more exactly the hypothetical center for movement by pricking the cord and medulla with a sharp instrument at progressively higher levels in order to stimulate them. His most important finding is as follows: [9]

> When I reached the neck, I was very astonished to see that pricking the cord produced no convulsions in the parts to which it sends nerves; on thrusting either a stylet or the point of a scalpel under the occiput, I excited convulsions, but be-

[6] *The Odyssey*, Book X. Parenthetically it may be noted that loose-minded Elpenor was less fortunate than bored Eutychus (Acts XX, 9-12), who suffered a similar accident, in that there was no apostle Paul in attendance at Circe's Palace.

[7] The Latin text of this passage is to be found in a footnote on p. 79 of Milne Edwards' *Leçons sur la physiologie et l'anatomie comparée de l'homme et des animaux*, Paris, 1879, v. 13.

[8] *Mem. Acad. des Sci.*, 1760, *3*: 277; *ibid.*, 1760, *3*: 344.

[9] P. 366.

tween the 2nd and 3rd vertebrae, far from producing the same effect, the animal died almost on the spot, its whole body trembled, the pulse and respiration absolutely stopped, and there was perfect paralysis of the vital functions, that is to say, complete death, although the same thing did not happen higher up or lower down, but in small animals only between the 2nd and 3rd, and between the 3rd and 4th cervical vertebrae, and between the 2nd and 3rd for animals of a larger size.

Lorry had not hit the respiratory center itself, but he had cut off from it the motor pathways to the diaphragm and intercostal muscles. With the paralysis of these muscles the most obvious respiratory movements ceased.

Legallois' contribution to the subject of the respiratory center is to be found in a small book whose full title is " Expériences sur le principe de la vie, notamment sur celui des movemens du coeur, et sur le siège de ce principe," published in 1812, two years before his tragic death by suicide. His interest in the subject had been aroused six years earlier while attending a confinement in his capacity as a physician. The peculiar circumstances of the case made him wish to learn just how long a foetus at term could live without breathing, and since books could not give him the desired information he began a long series of animal experiments to obtain first hand information. After finding that newborn rabbits do not die of asphyxia for a quarter of an hour, whereas older rabbits succumb in about two minutes, he was led to compare the effects of asphyxia with those of decapitation in the newborn rabbit. He says: [10]

All inspiratory movements of the thorax are abolished at the very instant of decapitation; the head alone preserves gasping movements which are exactly like those which take place in asphyxia. If, instead of decapitating the animal, one simply cuts the spinal cord between the occiput and the 1st vertebra, the phenomena are the same as after decapitation, viz. inspiratory movements of the thorax cease instantly, and the head conserves the gasping movements of asphyxia.

This observation was a long step in advance of Lorry, since by showing that after severing the entire cord from the brain there were still respiratory movements of the head in spite of the fact that thorax and diaphragm were paralyzed, Legallois proved that the seat of the urge to breathe did truly lie in the brain. This puzzled him greatly. He was quite aware that the nerves to the diaphragm and intercostal muscles come from the spinal cord in the same way that nerves are supplied to the muscles of the trunk, so why, he asked, should decapitation abolish some respiratory movements and leave others? He was unable to solve the

[10] P. 29.

riddle, but he did succeed in finding the anterior limit of this vital area. He says: [11]

> It is not on the entire brain that respiration depends, but only on a very circumscribed area of the *medulla oblongata* situated a short distance from the occipital opening and towards the origin of the 8th pair of nerves (the pneumogastric). For if one opens the skull of a young rabbit and extracts the brain in successive portions from front to back by cutting it in slices, one can in this way remove the entire cerebrum, then the entire cerebellum, and finally a part of the medulla without cessation of respiration. But it ceases suddenly when one includes in a slice the origin of the nerves of the 8th pair.

Flourens' contribution to the subject aside from the application of the term *noeud vital* was, as he himself said,[12] merely to fix in a still more precise manner the veritable site in the *medulla oblongata* of the primordial principle of the respiratory mechanism." His method of determining the limits of its extent was the one which had been used by all his predecessors, viz. making complete transverse slices across the medulla at different levels. In the rabbit he found the upper limit to lie immediately anterior to the origin of the vagi, and the lower limit three "lines" [13] posterior to the origin of these nerves. The exact extent of the area might vary slightly in animals of different sizes, but in any case it was essentially a point, since the distance between its anterior and posterior limits was never more than a very few "lines." Both Legallois and Flourens used the origin of the vagi as a landmark in locating the respiratory center, but it was evident that the vagi themselves were not essential. Marshall Hall (1790-1857) in England, however, claimed that although removal of the cerebral hemispheres or of the vagi would not abolish respiration, "if both are removed, the inspirations cease, as in the experiment of dividing the *medulla oblongata* at the pneumogastric nerves, an experiment hitherto unexplained." [14] This claim Flourens was able to disprove; [15] the loss of no single part of the brain or its nerves, nor any combination of parts or nerves would produce sudden cessation of respiration, unless the very special area of the medulla were included.

Originally Flourens had used the term *noeud vital* to mean the medulla as a whole, but since to him the chief function of this part of the central nervous system was maintenance of respiration, and since this function

[11] P. 37.
[12] *Recherches expérimentales*, 2nd edit., p. 198.
[13] A "line" = 1/12 inch or 2.12 mm.
[14] *Memoirs on the nervous system*, London, 1837, p. 87.
[15] *Recherches expérimentales*, 2nd edit., p. 204.

was restricted to a very small part of the medulla, in 1851 he narrowed the term down to mean what he often referred to as the "*point vital*," or "the primary motor point of the respiratory mechanism." [16] From this time on, *noeud vital* was accepted as being synonymous with what we now call respiratory center.

Flourens at this time was still working on the exact location and extent of this vital point. He claimed that in the rabbit it was no bigger than the head of a pin, and he located it for physiologists "at the point of the V of gray substance inscribed by the V of the pyramids or point of the pen" (*calamus scriptorius*). This description of the location of the *noeud vital* was unfortunate, for it was thought that he meant not only that the *noeud vital* lay superficially in this gray matter, but that it was more posterior than he had intended to indicate. Other investigators thinking they were following his directions were unable to duplicate his results,[17] so that eight years later he felt obliged to correct these erroneous impressions, claiming [18] that he had mentioned the V of the gray matter only as a landmark; the *noeud vital* itself lay deeper in the substance of the medulla; and that instead of saying "at the tip of the V of gray substance" which was merely the lower boundary, he should have said "beneath the V." To make certain that he should not be misunderstood this time, he published drawings of the rabbit's brain showing for the first time the location of the respiratory center (Fig. 1). The correction came too late, the impression was firmly fixed, and subsequent writers always quote Flourens as locating the *noeud vital* at the tip of the *calamus scriptorius*.

Flourens' next contribution was to show that the center was double; that one could make a slit between the two halves, or destroy either the right or left half without stopping respiration.[19] He had made this discovery by changing his technique. Instead of making complete transverse slices he now inserted into the brain a narrow double-edged knife, or better, a hollow punch, thus destroying or removing a small core of tissue. His final papers [20] on the subject had to do with the *noeud vital* in cold-blooded animals. The new point brought out here was that this type of animal, as exemplified by the frog, can survive destruction of the *noeud vital* for months, though during all this time there would not be the

[16] *C. R. Acad. Sci.*, Paris., 1851, *33*: 437.
[17] E. g., Longet, F. A., *Traité de physiologie*, Paris, 1848, v. 2, p. 206.
[18] *C. R. Acad. Sci.*, Paris, 1859, *48*: 1136.
[19] *C. R. Acad. Sci.*, Paris, 1858, *47*: 803.
[20] *C. R. Acad. Sci.*, Paris, 1862, *54*: 314; *Ann. des. Sci. Nat.*, 1862, *17*: 158.

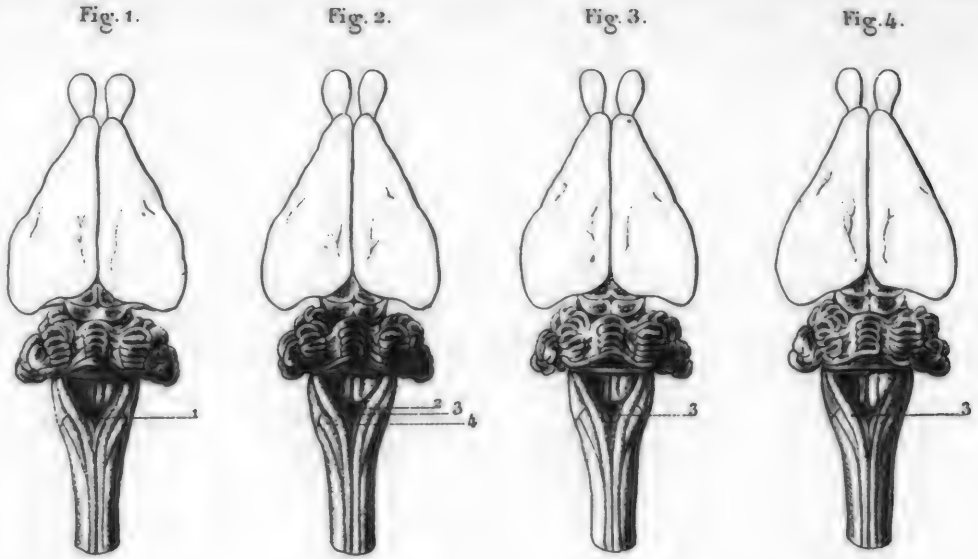
Fig. 1.
Fig. 2.
Fig. 3.
Fig. 4.
1
2
3
4
3
3
Fig. 1.
1. V de substance grise, marque indicatrice sous laquelle se trouve le nœud vital.
Fig. 2.
2. Limite sup.re du nœud vital.
3. Lieu précis où doit être faite la section du nœud vital.
4. Limite inférieure du nœud vital.
Fig. 3.
3. Lieu précis du nœud vital, détruit par l'emporte-pièce
Fig. 4.
3. Lieu précis du nœud vital, coupé par le scalpel à double tranchant

Fig. 1. Drawings accompanying Flourens' memoir of 1859. They are of interest not only because they were the first to depict the location and extent of the *nocud vital*, but also because they were drawn by A. Vulpian (1826-87) who at that time was Flourens' assistant and who later became one of France's most famous neurologists.

slightest sign of respiratory movements. Exchange of gases through the moist skin sufficed to maintain life in the animal.

Flourens by no means settled the question of the location and nature of action of the respiratory center. The subject is one of perennial debate and each generation of physiologists attacks it by use of the newest methods available, from the use of minute hot beads of the 1890's,[21] to valve amplifiers, oscillographs, loud speakers [22] and Clark stereotoxic instruments [23] of the present day. Flourens was certainly wrong in ascribing to the respiratory center a space no larger than the head of a pin. Longet (1811-71), a contemporary of Flourens, who repeated the latter's experiments shortly after they were reported, suggested on histological grounds that the center might lie in what we now call the reticular formation of the medulla,[24] and this was established later by Mislawsky.[25] We now believe that the two cell groups composing the respiratory center lie on either side of the central raphe of the medulla, not in a compact mass but scattered through the reticular gray matter from the level of the facial muscles over the cephalic four-fifths of the inferior olivary nucleus.[26] We have also become convinced that we can delimit one part of the center as controlling inspiration, and another as controlling expiration.[27] But as to the mechanism by which it maintains its automaticity and the exact way in which it functions one can still say as Legallois did a century and a quarter ago "This, to my way of thinking, is one of the great mysteries of nervous energy; a mystery which will be resolved sooner or later, and whose discovery will throw the most vivid light on the mechanism of the functions of this marvellous energy." [28]

[21] Gad, J. *Arch. f. Physiol.*, 1893, 175.
[22] Adrian, E. D., and Buytendijk, F. J. J. *J. Physiol.*, 1931, *71*: 131.
[23] Pitts, R. F., Magoun, H. W., and Ranson, S. W. *Am. J. Physiol.*, 1939, *126*: 673.
[24] Longet, F. A. *Anatomie et physiologie du système nerveux de l'homme et des animaux vertébrés.* Paris, 1842, v. 1, p. 398.
[25] *Centralbl. f. d. Med. Wissensch.* Berlin, 1885, *23*: 465.
[26] Pitts, R. F., Magoun, H. W., and Ranson, S. W. *l. c.*
[27] Pitts, R. F. *Am. J. Physiol.*, 1941, *134*: 192.
[28] Legallois, A. C. *l. c.*, p. 36.

DON GASPAR CASÁL, FRANÇOIS THIÉRY AND PELLAGRA

RALPH H. MAJOR

The names of Don Gaspar Casál and François Thiéry are linked together in the discovery of pellagra as are the names of Auenbrugger and Corvisart in the discovery of percussion. Corvisart realizing, after practice, the importance of Auenbrugger's discovery, remarked, " I could have raised myself to the rank of an author by revamping the work of Auenbrugger and publishing a work on percussion. But by that, I would sacrifice the name of Auenbrugger to my own vanity, that I do not wish to do. It belongs to him, it is his beautiful and rightful discovery (*Inventum novum*, as he justly says) which I wish to bring to life." With the same fine sense of integrity, François Thiéry, in his paper on Mal de la Rosa, which appeared in the *Journal de médecine, chirurgie et pharmacie* in 1755, seven years before the publication of Casál's observations, remarks that " M. Casál, physician of the Court, who adds to a taste for observation all the frankness of earlier times, who has practised medicine in the Asturias for twenty-five or thirty years and from whom I take the history I have just read; this wise observer, I say, assures me that the Mal de la Rosa has always resisted all remedies and that he regards it as incurable." Thiéry, who published in 1791 *Observations de physique et de médecine faites en différens lieux de l'Espagne*, quotes Casál on nearly every page of his chapter on the Asturias. The question of priority does not trouble Thiéry. Casál studied this disease for thirty years before he, Thiéry, even knew of its existence.

The biographical details of Casál's life are confusing and contradictory. Jourdan states that Casál was born in Oviedo, but this statement, according to Canella, " is entirely inaccurate." This error may have resulted from confusing Don Gaspar Casál with his son, Don Benito Ignacio Casál, who was born in Oviedo. François Thiéry, in his *Observations*, notes, " I have found numerous and accurate observations on this small part of Spain (Asturias), in the manuscripts and the conversation of Don Gaspard Casál, physician to the court: sincere friend of truth, he has studied well this country where he has practised during twenty-five to thirty years. Besides he was born in Aragon and in the beginning practised medicine in several places, especially at Medina-Celi, that is, on one

of the most elevated parts of the plateau of Castille." According then to his friend Thiéry, Casál was born in Aragon. Other friends and disciples, however, give conflicting testimony.

Pérez de Escobar, a celebrated physician born in Alcarria, speaks of Casál as his "countryman," an error probably due to the fact that Casál practised at one time in the region of Guadalajara. The historian, Catalina Garcia, states that he was a native of Gerona and could not be considered a son of Guadalajara. The province of Guadalajara adjoins that of Madrid while Gerona lies east of Barcelona. Garcia based his assertion on the records of the University of Siguenza which state that Casál was a native of Gerona and on the list of baptisms at the Cathedral of San Tirso in Oviedo, which records the baptism of Pablo Casál, "son of Don Gaspar de Casál, native of the city of Gerona."

The confusion increases when we find in his last will and testament that he is described as a "native of Utrilla, diocese of Siguenza." Siguenza is in the province of Guadalajara. To add to the confusion, the baptismal record of the church of Our Lord of the Valley in Utrilla, describing the baptism of a younger brother of Gaspar Casál in 1686, describes him as "Juan Martin, son of Federico Casál y Dajon, native of the city of Pavia in the State of Milan." This clearly describes the father of Gaspar Casál as a native of Pavia, and since Gaspar was born seven years before Juan, it raises the interesting speculation whether Gaspar Casál himself were born in Italy.

Thus, according to various authorities, Gaspar Casál was born in Oviedo in the Asturias; in Aragon; in Alcarria; in Gerona in the province of Catalonia; in Utrilla, a town in Guadalajara, and finally even in Italy. Morejon, the Spanish medical historian, sums it all up briefly, "We do not know for certain the place of his birth, or if he was a Castilian." He adds for good measure, "Neither do we know positively in which university he pursued his studies."

Gaspar Casál was born about 1679. In 1707, at the age of twenty-eight, he was practising medicine in the villages of Alcarria and possibly "reading medicine" with his friend Dr. Rodriguez Luna of Atienza. We do not know where he had studied medicine before he began to practise, but there is documentary proof that he entered the University of Siguenza as a student in 1709. Here again the data is confusing, for in 1713, at the age of thirty-four, he received the degree of bachelor of arts. Gaspar Casál's name does not appear among the graduates in medicine at Siguenza although his son received the degree of bachelor of medicine there in 1752. Although Casál received a degree in arts and not in medi-

cine at Siguenza, it is probable, as Canella remarks, that he also followed courses in medicine at this university. Incidentally, this school of medicine did not enjoy a very high reputation in the seventeenth century, for we find Cervantes in his immortal *Don Quixote* describing in a mocking tone "a fellow, learned graduate of Siguenza" who was called to treat Argamasilla.

The same year Casál received his degree in arts at Siguenza he settled in Madrid to practise medicine. Although his professional education may have been somewhat irregular, and he does not seem at that time to have had a doctor's degree, he soon developed a good practice and numbered among his patients many influential personages at court. Four years later, he was appointed city physician to Oviedo in the Asturias where he practised medicine for thirty-three years.

In 1751, Casál withdrew from Oviedo and established himself at the court in Madrid. Soon thereafter he was named "supernumerary" physician of the Royal Chamber, taking the oath on September 17, 1751, and almost immediately was admitted to membership in the Royal Academy of Medicine. It was during this period that François Thiéry, a young French physician, made the acquaintance of Casál. Thiéry, who was born in 1718, was greatly interested in the influence of climate on health and disease and travelled extensively in order to study these influences. He spent three years in Spain studying the various climates and diseases and found in Casál a kindred spirit as well as a mine of information.

Casál, in 1752, was made Protomedico of Castille. Seven years later on August 10, 1759, Casál died, having reached the advanced age of eighty.

Casál's fame was well established in the Asturias by the long years of service he had rendered the inhabitants of that province. During these years he had made careful notes regarding the topography and climate of the Asturias, its villages, waters, minerals, trees, food, atmosphere, winds and diseases. These notes were bequeathed to his faithful friend, Dr. Juan Joseph Garcia Sevillano, who arranged them for publication. Three years later, in 1762, Casál's posthumous *Historia Natural y Medica de el Principado de Asturias* was published in Madrid, a work which spread his fame far beyond the confines of the Asturias or, even, of Spain itself.

Casál's book begins quite properly with a chapter on the topography, followed by a chapter on the towns of the province. This latter chapter is followed by an appendix on the diseases that prevailed during the year 1720. He then proceeds to discuss in succeeding chapters the waters, the

mineral springs, the minerals and metals, the trees and plants, vegetables and meats, atmosphere, winds, temperature. These chapters take up some ninety pages of Casál's book. On page 92 the author takes up the purely medical aspects of the Asturias and the following three hundred pages are devoted to a description of the diseases he saw in the Asturias, usually with illustrative cases.

Casál describes lombrices, renal calculi, long continued fevers (probably typhoid), ulcers of the legs, cachexias, hysterical passions and epilepsy. At this point, a section is rather abruptly inserted on the important doctrines and sentences of Hippocrates, with commentaries by Casál and illustrative cases from his practice in the Asturias. After this diversion, the author proceeds to a long chapter of nearly two hundred pages in which he describes the epidemic diseases which he saw between the years 1719 and 1721.

The reader would expect Casál's *Historia Natural y Medica de el Principado de Asturias* to be written in the Spanish language but after some three hundred pages of Spanish, a section begins " Historia affectionum quarumdam Regionis hujus familiarium " and the remaining one hundred pages are written in Latin. In this section, Casál describes scabes, leprosy, and finally, writes what is to his successors the most interesting section in his book, " De Affectione, quae Vulgò in hac Regione mal de la Rosa nuncupatur " (Concerning the affection which in this region is commonly called mal de la Rosa).

" Since I have observed carefully," Casál writes, " in many years of practice all the symptoms common to this disease and I saw in this region none of all the indigenous affections more horrible or more refractory, I have decided it would not be out of place for me to write a history of it.

" And although thus the numerous symptoms of this disease may be very distorted (however it may agree with what is said below) itself moreover only one of them, took itself that common name: and this terrifying crust is a certain symptom, which may have at first only a reddish appearance and causes the underlying parts to be rough; it degenerates then into a very dry, scabby, blackish crust; deep fissures very often appear, penetrating to the living flesh, with extreme pain, burning and discomfort.

" This loathsome crust (from which the disease is called mal de la rosa) adheres firmly to the metacarpals and metatarsals of the hands and feet. No other affection of this kind or nature has appeared in this region without such a crust in certain areas. Thus, crusts may appear on the soles of the feet, the palms of the hand, elbows, arms, head, face, stomach,

HISTORIA
NATURAL, Y MEDICA
DE EL PRINCIPADO DE ASTURIAS.

OBRA POSTHUMA,

QUE ESCRIBIO EL DOCT. D. GASPAR Caſál, Medico de ſu Mageſtad, y ſu Proto-Medico de Caſtilla, Academico de la Real Academia Medica Matritenſe,&c.

LA SACA A LUZ

EL DOCT. JUAN JOSEPH GARCIA Sevillano, Medico de Familia del Rey nueſtro Señor, Ex-Examinador de ſu Real Proto-Medicato, Medico que ha ſido de los Reales Hoſpitales, y actual de el Real Sitio de Buen Retiro, Academico de la Real Academia Medica Matritenſe, y de la Real de Oporto, &c.

CON LICENCIA: En Madrid, en la Oficina de Manuel Martin, Calle de la Cruz. Año de 1762.
Se hallarà en la Libreria de Don Franciſco Manuel de Mena, Calle de las Carretas.

1. Title Page of Casál's *Historia Natural y Medica de el Principado de Asturias.*

thighs, or legs and continue red, rough and erysipelatous, besides being accompanied by other symptoms of the disease de la rosa; verily it is not yet called mal de la rosa, unless the crusts described above appear obviously first in the metacarpals or metatarsals. Now it should be known, these crusts most commonly make their appearance about the Spring equinox, rarely at any other time. In summer they are apt to slough off (perhaps because of sweat), the tissue beneath being entirely free of all pustules and crusts. Indeed, in the spot which they occupied, reddish stigmata remain, extremely shiny, like the scars which healed burns leave. Thus the skin of the metacarpals and metatarsals, that part where the crust formerly was, even though it had been rough, wrinkled and shaggy (as often happens in old people) now appears bright, smooth and without wrinkles; the remaining skin appears a little lower, or more depressed. It is very probable that the name *rosa* takes its origin from this red color and brightness of the scar."

Casál proceeds next to describe a series of typical cases. "The 26 of March 1735, a certain individual of forty years, who complained of this disease, came to consult me, and in correct and elegant language related to me the following:

"It has happened that he complained on occasions of certain fevers like the epherema. He did not lose his appetite entirely, but after dinner he immediately became sleepy, which lasted then for a time as if he were a stupid person, and especially in the month of March. A few times he was troubled with thirst, he felt continually a certain fatigue or better a weakness in his extremities, especially the lower extremities. When he walked around or took any other kind of violent exercise, suddenly he was confused and mixed up in his head in such a manner, that if he did not stop immediately he tottered and could not avoid falling; and it should be noted that this happened without losing his senses. He walked always carelessly and lazily. He was always bothered with a bitter taste in his mouth. He could not stand cold weather, it tormented him terribly. When he was still he had constantly his feet frozen, if he walked they felt like fire.

"His wife had the same disease; in addition to the common symptoms which she herself confessed tormented her, there was one that tormented her above all, she could not endure heat, or sun, nor fire because of the terrible headache these things caused her: neither could she endure cold, because she felt it penetrated her body in such a way, that it passed through her innermost organs. Every year, a little before the equinox of Spring, there appeared on the metacarpals and metatarsals of the hands

and of the feet, horrible crusts, when the heat of the summer solstice came they separated and fell off, the scar remaining."

After relating several other cases, Casál then discusses the principal symptoms of this disease which he says are seven in number: "(1) The constant trembling of the head, which although it is common to all patients, it is in many so lasting they are not a single moment without an irregular movement of the entire body. In the hospital of Santiago, of this city, I cured a little woman (and if necessary, I would swear it under oath) whose body, especially the upper half, was balanced like a swallow pushed by a varying wind; in order to hold herself steady, she had to move her legs very fast, to prevent herself from falling down to the ground at any moment, (2) the burning pain of the mouth, vesicles on the lips, and a coating on the tongue, (3) the distressing weakness of the stomach and the weakness of the entire body, especially of the legs, and a strange laziness and carelessness, (4) the crusts of the metacarpals and metatarsals and a sort of collar on the upper part of the neck, (5) the scorching heat which torments them, especially in the chest, (6) that smoothness or delicate fineness of the skin which does not resist either heat or cold; and (7) the heaviness, which without any known cause, attacks them and causes them to give way to a sad crying, a phenomenon which by itself is a pathognomonic sign of the affection."

Casál, like the true disciple of Hippocrates, was much puzzled as to the origin of this disease. "Is the cause of this disease to be sought in the Heavens, that is in the condition of the atmosphere, or in constitutions, or in the diet of the patients?" He turns first to the diet and finds that maize is the principal article of diet and that fresh meat is rarely eaten. However, they have eggs, chestnuts, beans, milk, butter, cheese, apples, pears and nuts. "Now nearly all who were seized by this disease are poor peasants."

Further investigations by Casál increase his perplexity. He finds that the diet of the peasants is practically the same throughout the entire province, yet the cases of *mal de la rosa* are not evenly scattered throughout the provinces but are mostly in four communities. He seemed at first to be impressed by the fact that his patients ate so little meat but, on reflection, he recalled the case of his old friend and patient, Joannes Baptista Dolado, who never ate meat or fish but only bread, legumes, fruit and cheese, yet reached the ripe age of eighty.

Casál leaves us in doubt regarding the etiology of this disease and does not devote much space to therapy. François Thiéry in his communication published in Paris, as previously mentioned, says that Casál

2. Illustration of Patient Suffering from Pellagra. From Casál's *Historia.*

" assures me that the mal de la Rosa has always resisted all remedies and that he regards it as incurable." We have no criticism of Casál's failure in discovering the etiological factor or the cure of disease. Two centuries later, we stood almost where Casál did.

The modern term for the mal de la rosa was first used by Francesco Frapolli, who employed the term long used by the peasants of Lombardy—pellagra. Frapolli's *Animadversiones in Morbum, vulgo Pelagram*, which was published in Milan in 1771, states that pellagra " is indeed judged a new disease; for no one, whom I know myself, has up to the present time written particularly concerning this affection of the skin." Frapolli was apparently quite unaware that a classic description of this disease had been published by Casál nine years earlier.

In the years 1786 and 1787, twenty-seven and twenty-eight years after the death of Casál, the Reverend Joseph Townsend, rector of Pewsey, Wiltshire, travelled through Spain. After his return, he published his observations in a three volume work with the title, *A Journey Through Spain*, in which, as the full title indicates, he devoted " particular attention to the agriculture, manufactures, commerce, population and revenues of that country."

Townsend, an acute observer, saw, in the Asturias, pellagra, which he describes as " a disease peculiar to this province, called *Mal de la Rosa*." " The *Mal de Rosa*," he continues, " has been considered as a species of leprosy; but to me it appears to have no affinity with that disease. It attacks the back of the hands, the insteps, and the neck, where it descends to the sternum, almost to the cartilago ziphoides, but the rest of the body is free. At first it appears red, accompanied with pain and heat, but ends in scurf. In the progress of this disease, vertigo and delirium succeed, with foul tongue, lassitude, chilliness, tears, and, according to the testimony of Dr. Durand, a peculiar propensity to drown themselves. It goes away in summer, and returns in spring. The disease may be cured by nitre and gentle cathartics; but if neglected, it terminates in scrophula, marasma, melancholia, and madness." This is an excellent thumbnail sketch of this disease, but, as physicians, we desire definite accounts of patients " cured by nitre and gentle cathartics."

Townsend describes in some detail the diseases he saw in the Asturias and, with commendable frankness, states, " This account, collected from gentlemen of the profession, is confirmed in the valuable work of don Gaspar Cassal, an old physician, of more than common observation and experience, who has given to the public a natural history of the Asturias." Townsend, in concluding his observations on the Asturias, remarks,

" Although subject to such a variety of endemical diseases, few countries can produce more examples of longevity. Many live to the age of a hundred, some to a hundred and ten, and others much longer."

François Thiéry, as previously mentioned, published the first account of pellagra in 1755, and in 1791 his *Observations de physique et de médecine faites en différens lieux de l'Espagne* appeared. This work resembles Casál's *Historia Natural* in many respects and quotes Casál constantly in his discussion of the diseases of the Asturias. Thiéry enjoyed a splendid reputation in France and had a vast practice in Paris.

Thiéry's description of pellagra adds little to that of Casál. In discussing the name of the disease, Thiéry notes that after the scabs and pustules have disappeared " there remains in their place stigmata which are red, glossy, shiny, denuded of hair, even in the aged, more depressed than the surrounding skin, quite similar to the scars left by burns on healing. It is probably the red and glistening color of these stigmata which has given this disease the name of *mal de la rosa*." Thiéry quotes with approval Casál's observation that this disease never affects the rich and is seen only among the poor who live mainly on corn. He quotes Casál's opinion that a diet richer in fats is beneficial and quotes one of Casál's cases, that of a woman who in her delirium begged for butter, which, when given her, cured both the delirium and the mal de la rosa.

The observation that pellagrins subsist mainly on corn, as first noted by Casál and confirmed by Thiéry in Spain, was later noted by Frapolli in Italy and by other observers in different countries. Pellagra, according to the first edition of Osler's *Practice of Medicine*, published in 1892, " has not been observed in this country." The sixth edition, published in 1907, repeats this statement, but this same year Searcy reported a large number of cases of pellagra in an asylum in Alabama, the victims living mainly on corn.

Casál was a great admirer of Hippocrates and never tired of quoting him. His countrymen referred to him as the Spanish Hippocrates. Certainly he was imbued with the Hippocratic spirit and the Hippocratic method. He described the mal de la rosa with great fidelity; he noted its prevalence among the poor; he stressed the dietary deficiencies of its victims, but " had no need of an empty supposition such as occult and doubtful things, which, if one wishes to discuss he must employ hypotheses " (Hippocrates). Casál's *Historia Natural* was a worthy successor to *Airs, Waters and Places.*

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STUDIES ON MORTALITY SINCE THE RENAISSANCE*

SIGISMUND PELLER

D. Twins and Singletons.

In the third part of this series the mortality of all children was studied, regardless of whether they were single born (singletons) or twins. In this part we will focus our attention on multiple births.

The mortality of twins is of interest to us for three reasons. On account of an unfavorable intrauterine environment twins more frequently are premature and underdeveloped than are singletons. The question therefore arises as to how much of the damage done by the intrauterine conditions can be repaired by care. The literature on this subject is rather poor. Much more work has been done on the genesis, the intellectual development and on the significance of twins for the study of heredity than on later survival rates (see H. H. Newman (1), N. D. Hirsch (2)). Secondly, the birth of twins has been associated with high potential and actual fertility and has been linked with maternal heredity; twins themselves have been considered rather of low fertility. All this suggests constitutional deviations of twins from the average type and perhaps deviations in viability which could become manifest after the intrauterine damage has been overcome. Third, a historical approach might help to elucidate whether social conditions having a bearing upon growth and physiology of the female body, do influence intrauterine mortality of twins in early stages of gestation, and by this the apparent frequency of twins at birth time.

Historical Review.

In a communication to the Royal Society, London, in 1788, J. Clarke (3) stated that in the Lying-In Hospital of Dublin, in the years 1757-1784, there were born 331 pairs of twins among 20,117 newborns, giving a proportion of 1 pair to 59 confinements. Of all newborns, 3.33% were twin individuals. Half a century later, analysing 129,172 deliveries of the same hospital, Robert Collins (4) remarked that the proportion of twins to all deliveries in Ireland (1:62) is higher than in Germany (1:80), Scotland and France (1:95), or in England (1:92). He thus confirmed A. v. Haller's assumption that national and geographic factors

* Continued from this *Bulletin*, vol. XIII, No. 4, April 1943, pp. 427-461.

have a bearing upon the frequency of multiple births.[1] Since then the existence of great differences between countries has been repeatedly established. For 1921-25, Prinzing (5) calculated the proportion of one pair of twins to all deliveries to be in Denmark 1:62, in Norway and Sweden 1:68, in Switzerland and the Netherlands 1:74, in Germany 1:83, in Italy 1:86, in Hungary 1:88, and in France 1:91. In the U. S. A., for 1926-1930, 1931-1935, and 1939 and 1940, one pair of twins was reported per 86, 87 and 93 deliveries, respectively. Different degrees of accuracy in recording multiple births in various countries does not account for the wide range in the proportions shown here. Twins seem more frequent among whites than among Mongoloids, and in the U. S. A. twins are more frequent among Negroes than among whites.

In the 18th century, von Haller (6) linked the genesis of multiple births with abundance of eggs simultaneously available for fertilization. Haller discussed superfecundation and superfetation. He considered quintuplets the largest litter size in man.

According to L. Kleinwaechter (1871 (6a)), in the eighteen-thirties and forties, the genesis of twins was connected with the rupture of two Graafian follicles in one menstruation (Bischoff, 1842), with the existence of two eggs in one follicle (Baer) and also with two preformed "Keim Anlagen" in one egg (Barry, 1839). Thus the idea of splitting twins into fraternal and uniovular is now over 100 years old.

Multiple births of the fraternal type were associated with the retention of eggs ripened during pregnancy (A. Puech, 1874), with increased innate fertility (Duncan) and with a reduced physiological involution of Graafian follicles in some adult women, so that more than one follicle simultaneously complete ripening up to the expulsion point of the egg (D. Hellin, 1895 (7)). With the advancement of modern endocrinology, explanation of multiple pregnancies was sought in a disturbed hormonal mechanism. C. Zeleny (8) assumed that hormones normally prevent the ripening of more than one Graafian follicle within one menstrual period. G. Dahlberg (9) gave that hypothesis a more definite form. According to that author, several follicles prepare simultaneously for expulsion of their respective eggs, some of them being quick in the process of ripening, others slow. From a certain stage of development on, the follicle cells produce estrin that kills the eggs in those other follicles which took part in the race of ripening but were too slow to reach that certain stage. Thus, as a rule only one egg becomes available for impregnation. How-

[1] Called also plural births.

ever, if by chance more than one follicle reached that certain stage of development at the same time, then the respective second, or second and third egg (and so on) survive the estrin action upon them and are available for fertilization. The result is a pair of twins, or a set of triplets, quadruplets or quintuplets.

C. B. Davenport (12) made the assumption that within each intermenstruum several follicles burst but of several expelled eggs either one only becomes fertilized or, if more have been fertilized, only one survives the action of letal factors carried by the spermia. This conception was modified by Lenz, according to whom the fertilized egg secretes a substance that prevents other eggs from being fertilized. Men whose spermia lack the ability of inducing production or liberation of that substance, become fathers of fraternal multiple births. Neither of these two hypotheses has been sufficiently supported.

Just as nations vary with respect to frequency of twins, so also do families. The familial inclination apparently is limited to fraternal twins and has been explained by maternal heredity. Analyzing family records of Stuttgart for about one century, W. Weinberg (10) found in relatives of mothers of fraternal twins the frequency of the latter to exceed expectation by 1.5 times while in case of presumably uniovular twins expectation coincided with the actual figure. Occasionally also involvement of paternal heredity has been assumed for all twins (V. Goehlert, 1879 (11), E. Strassmann, Guillemot, C. B. Davenport (12)), or only for uniovular twins (S. Rosenfeld (13)).

In 1902, W. Weinberg (10) pronounced the rule that only one half of the dizygotic twin pairs should be of opposite sex. Thus, the number of monozygotic twins is equal to the difference between all like-sexed pairs and the number of opposite-sexed pairs. Prior to this only about 12% of all twins were considered monozygotic; Weinberg assumed a figure about twice as high. If the mathematical reasoning was correct, the conclusion was justified that examination of the partition membranes as to the number of layers as well as the single-placenta-test are not infallible.[2] Later studies on placental and membrane relations (O. Grosser, 1927; Fr. Curtius (14)) proved that point. Mistakes are possible in both directions. Monozygotic twins may be mono- or dichorionic. If the

[2] J. Spaet (1860) was the first to study similarity with respect to uniovular and twoovular twins on a large number of newborns. Spaet used the placenta and the membranes for the classification. Later on Fr. Galton tried classification of twins on the basis of similarity. In a long series of papers F. Schatz (1882-1910) demonstrated that similarity of twins depends on their age, becoming more outspoken in uniovular twins and diminishing in fraternal pairs.

division of the embryo takes place early, each of the uniovular twins may have his own amnion, chorion, placenta and umbilical cord, just as in the case of binovular twins. On the other hand, binovular twins may present a placenta and membranes as uniovular twins do. Furthermore, von Verschuer's studies (1932) disclosed also that the physical characteristics of twins are not an absolutely reliable method of differentiation between mono- and dizygotic twins.

Weinberg assumed that the frequency of uniovular twins is about equal in all countries, nations and races, while the incidence of binovular twins differs. The rarity of twins in Japan would be due to the low frequency of binovular twins (T. Komai and G. Fukuoka (15)).

A considerable number of investigations on characteristics of homozygotic twins in man, such as their lower vitality or their independence of the age of the mother or the order of birth, is based on Weinberg's mathematical reasoning as to the proportion of uniovular to binovular twins in the sum total of multiple births officially reported. Yet, it may be doubted whether—as far as man is concerned—the calculations are correct, since the existence of uniovular twins and their genesis has not been definitely established. So far there is no sign or symptom at our disposal which in case of like-sexed twins could rule out the two-ovular genesis. The diagnosis is rather a matter of probability based on the degree of likeness in the combined features of the twins. The experience that in armadillos uniovular quadruplets often markedly differ among themselves, should make one cautious as to the value of similarity.

At variance with Barry's conception, at present uniovular twins are not supposed to result from a preformed "Anlage" in the egg. It is the sperm which either induces early fission of the blastodisc or produces a tendency to secondary budding and thus becomes responsible for the genesis of uniovular twins. A modern version of Barry's conception is connected with the name of the English statistician, R. A. Fisher (16) who, based on Thorndike's measurements, considers twins a homogenous group of uniform origin. According to Fisher, the differentiation into identical and fraternal twins is not warranted and each pair of twins arises from one ovum split after maturation into two identical portions, each of which became fertilized by a separate spermatozoon. That hypothesis found only little support and, as far as this mechanism has been accepted, applies only to the genesis of intermediate uniovular twins, as a distinct third group of twins (M. Th. Macklin, 1940).

Early in the 19th century investigators became interested in the numerical proportion between singletons, twins, triplets, quadruplets and

quintuplets. Sickel (1859) analyzing 17.7 million births, found one pair of twins per 83 deliveries, one set of triplets in 8,077, and one set of quadruplets in 385,499 deliveries. Veit's (1855, (17)) figures were close to Sickel's (1 : 89 and 1 : 7, 910). Also Wappaeus' (1859) figures showed a certain regularity in the numerical proportion of singletons to twins and triplets (1 : 86, 1 : 7, 400). Apparently D. Hellin (1895) was the first to realize the rule behind that regularity. If $B/T = n$, where B is the total of births and T the corresponding number of pairs of twins, then n indicates the number of births per one pair of twins. The statistical studies disclosed the fact that if $1 : n$ is the proportion of one pair of twins to n births, $1 : n^2$ gives the proportion of one set of triplets to the number of births, $1 : n^3$ represents the number of births among which one set of quadruplets is to be found, and $1 : n^4$ gives the number of births corresponding with one set of quintuplets.

Hellin's book was not obtainable, therefore I must rely on the authority of H. H. Newman (12) in the assertion that Hellin formulated these proportions in terms similar to those just mentioned. Apparently Hellin's law was forgotten and rediscovered 26 years later by C. Zeleny. Since then, the law has been checked and tested several times. Some authors, among them Greulich (18) and Guttmacher (19) expressed themselves in favor of the rule, while others, among them R. Pearl (20) have been rather inclined to discard the Hellin–Zeleny law on account of small deviations of the actual figures from it. How small these deviations are may be shown on U. S. A. statistics for 1939/1940. In these two years, 4,620,000 children were born, among them 49,884 pairs of twins, giving thus a proportion of 93 : 1 ; n being 93, the total number of births (B) divided by n^2 and n^3, respectively, indicates the number of expected sets of triplets and quadruplets, namely 535 and 6 respectively. The actually recorded figures were 521 and 5. Considering that sets of multiple births in which all individuals were stillborn have not been recorded, the deviations from the rule are surprisingly small.

Collins, Duncan and later, Goehlert have recognized that frequency of multiple births is a function of the order of births and of the mother's age. J. Bertillon (21) corroborated these findings, analyzing St. Petersburg's statistics, and Dahlberg as well as Guttmacher, and Yerushalmy and Sheerar (22) have inferred that these relations are true only for binovular twins.

TABLE 1. PERCENTAGE OF PLURIPARAE ACCORDING TO MOTHER'S AGE.

Age of the mother in years	Dublin, Hospital 1826–1833	St. Petersburg 1882–1892	U. S. A. 1940
15–19	.3	.6	.6
20–24	1.1	1.0	.8
25–29	1.4	1.4	1.1
30–34	1.8	2.1	1.4
35–39	2.3	2.1	1.7
40–44	2.1	1.6	1.4
45–		1.8	.9

Twins in Ruling Families

The first attempt at utilizing records of ruling families for the study of twins was made by V. Goehlert (11). Sex composition and heredity of twins as well as their relationship to the age of their parents and the twin mortality were scrutinized. The investigation has failed for several reasons, one of them being a great amount of mistakes (H. Naegeli–Åkerblom (23)). At the beginning of this century, S. Rosenfeld (13) tried to utilize about 150 years of births recorded for German nobility. This material was incomplete.

In our study based on C. von Isenburg's tables (25), we limited the analysis to those 1610 fertile women who married between 1500 and 1920[3] and had a total of 8,506 deliveries. There were 85, and perhaps 87 pairs of twins born by 81, and perhaps by 82 women.[4] Dividing 8,506 by 85 or 87, one gets 100 or 97.5, respectively, which if squared, according to the Hellin–Zeleny rule, gives the number of deliveries corresponding to one set of triplets. That number is 9,506 to 10,000. Since the material here considered is smaller, we are not surprised about the absence of triplets.

In this as well as in all calculations of the other investigators, deliveries of single and of multiple births were taken as units of operation. Let us now change the calculation and use as a unit the number of women instead of deliveries. Such a procedure changes the proportions and the meaning of them. Although the material at our disposal is small, that change widens the scope of the studies on quantitative relations between the

[3] For some calculations also marriages of 1921-1930 have been utilized. Where this was done, it will be noted.

[4] In one case the data are incomplete for the decision whether or not this woman had twins; in the other case the woman had one pair of twins and later most probably also a second pair, but the data for the second pair are not complete enough for a definite decision.

frequency of single and multiple births. If W_f symbolizes fertile women and W_t is the number of women who had born twins, then $W_f / W_t = m$ indicates the number of fertile marriages in relation to marriages producing twins. Thus, in our sample with 1,610 fertile women, $m = 1610/81.5 = 19.75$, and $1 : m$ symbolizes the proportion of mothers of twins to all fertile women. Dividing the total of 1,610 fertile women by m^2 one gets $1610/390 = 4.13$ which, if chance alone is decisive, indicates the number of women expected to have had twins twice. Actually there were 4, or perhaps 5 such women. For the fifth mother, as was pointed out above (see footnote), the data makes a second pair of twins probable but not certain.

To repeat, in this calculation every fertile mother was counted once, regardless of the number of deliveries, while all investigators who followed Hellin–Zeleny regarded the delivery as a unit, not the mother. Therefore in their studies n is a value between 62 and 93, while here $m = 19.75$. While the proportion $1 : n^2$ gives the expectation of *triplets* in a total of deliveries, the proportion $1 : m^2$ indicates the relative frequency of women with *more than one pair of twins*.

Applying the same procedure to Weinberg's families with 1,586 mothers of twins and 93 women with more than one pair of twins, and taking into consideration that according to this author every 14th to 23rd fertile woman was a mother of twins, I found the figure 93 complied with my formula $1 : m^2$. With regard to Goehlert's first study (1868) comprising 2000 marriages and 128 mothers of twins, 10 mothers had twins twice, whereas according to the formula $1 : m^2$ eight mothers were to be expected. I did not investigate whether the difference between 10 and 8 is real.

Now, the frequency of multiple births of various litter size and combinations in one woman, can be presented in three terms of which n and m are already known, and c denotes the number of children per fertile woman who passed the age of reproduction. All data are to be derived from the series: m, $m(m.c)$, $m(m.c)^2$, $m(m.c)^3$, $m(m.c)^4$, each term representing the number of mothers of whom *one* had born the respective set of multiple births, from twins to sextuplets. Setting $m.c = p$, the series gets the simplified form: m, $m.p$, $m.p^2$, $m.p^3$, $m.p^4$. Several of the interrelations may be shown in the following table. In that table's right column approximations in absolute numbers for the last 150 years are given on the assumption that for that time m was 20 mothers and c was 4 children.

These calculations represent expectancy if no or only a slight degree of hereditary tendency to repeated delivery of multiple births is involved. The here demonstrated approach makes us expect women with two pairs

TABLE 2.

The number of fertile women among whom one woman had	In terms of m	In terms of n	Remark: provided m = 20 and c = 4
1) twins	m	n/c	1:20 mothers
2) twins twice	m^2	$(n/c)^2$	1:400 mothers
3) triplets	$m^2.c$	n^2/c	1:1,600 mothers
4) twins three times	m^3	$(n^2/c)^3$	1:8,000 mothers
5) triplets and twins	$m^3.c$	n^3/c^2	1:32,000 mothers
6) quadruplets	$m^3.c^2$	n^3/c	1:128,000 mothers
7) twins four times	m^4	$(n/c)^4$	1:160,000 mothers
8) triplets twice 8a) quadruplets and twins	$m^4.c^2$	$(n^2/c)^2$	1:2.56 million mothers
9) quintuplets	$m^4.c^3$	n^4/c	1:10.24 million mothers
10) quadruplets and triplets 10a) quintuplets and twins	$m^5.c^3$	n^5/c^2	1:205 million mothers
11) sextuplets	$m^5.c^4$	n^5/c	1:820 million mothers
12) quadruplets twice 12a) quintuplets and triplets 12b) sextuplets and twins	$m^6.c^4$	$(n^3/c)^2$	1:1640 million mothers

of triplets to be as frequent as women with one set of quadruplets plus one set of twins. Furthermore, women with quadruplets should be more frequent than mothers of one set of triplets and two sets of twins (m^4c). Mothers of quadruplets and triplets are expected to be as frequent as women with quintuplets and twins. According to the Table 2, within the last 150 or 160 years not more, and rather less than 6 mothers of sextuplets had to be expected, whereas, according to H. H. Newman, the foremost research worker in the field of twins, 4 certain and 2 possible cases have been reported.

The order of frequency of some combinations is reversible as it depends on the value c. Thus, mothers of quadruplets should be more frequent than mothers of 4 pairs of twins as long as the average number of children is 4 or less, but less frequent if the average number of children is 5 or more.[5]

Let us now return to the study of the ruling families. In the 437 years

[5] I do not enter in a discussion of formulas which would help to divide multiple births according to the number of ova involved and according to the combination of mono-, di-, and trizygotic sets. Those interested in this side of the problem should read R. L. Jenkins and J. Gwin (24).

under study, the age distribution of mothers at the time of a twin delivery changed considerably. In the first two hundred years, about one half of all twins were born to women 25-34 years of age; in the 18th century one half of the twin mothers were 20-29 years old, and in the most recent period of 137 years one half of them is found in the age group 20-24 years. Correspondingly also the fathers became younger.[6] These changes are not surprising in themselves, as the reproductive activity of older women became more and more restricted and the birth decline in ruling families started as early as the 18th century.

TABLE 3. RULING FAMILIES; MOTHERS OF TWINS† ACCORDING TO AGE.

Mother's age in years	Marriages of the 16th and 17th centuries	18th century	19th and 20th†† centuries†	all 430 years
–19	2	—	—	2
20–24	9	6	8	23
25–29	13	4	4	21
30–34	12*	5	2	19
35–39	11**	3	1	15
40–	2	—	—	2
?	5	—	—	5
all	54	18	15	87
all fertile women	808†††	364	483††	1655

† incl. the two probable cases.
†† up to 1930; 45 women married 1921–1930.
††† among them 204 cases of unknown age
* among them 1 probable case of a twin mother
** among them 1 probable case of a mother of two twins.

Perhaps the changes in the age distribution as shown in Table 3 are not fully explained by the birth decline in older women. In young women twins became rather more frequent than they were in the 16th and 17th centuries (age below 25 years: 14 versus 11 pairs of twins).

In the 16th, 17th and 18th centuries women who have been delivered of twins had an excess fertility of 3 to 3.5 children as compared with all contemporaneous fertile women of the ruling families. The figures were: 8.7, 9.0 and 8.5 children versus 5.7, 5.8 and 5.0 children, respectively. Later, in the 19th century, the difference shrank considerably (4.75 versus 4.5 children) and disappeared almost completely in the 20th century. Women who had married 1900-1920 and became mothers of twins

[6] In the three respective periods, there were over 35 years of age: 31 out of 54 fathers, 9 out of 18, and 6 out of 15 fathers.

had an average of 4.5 children, whereas the other fertile women had 4.4 children on the average. This shrinking of the difference in fertility suggests that women with an innate tendency to higher fertility have learned to utilize birth control to a higher degree than the other women of the same social strata.

The chances of the first conception resulting in the delivery of twins always have been relatively small. This definitely places the mother's role in the occurrence of twins above the father's. Of 1,655 first born children,[7] 18 or 1.1 ± 0.2% were twin individuals, whereas the corresponding value for 6,851 children of higher order of births was 156 or 2.3 ± 0.1%. The probability of a first conception ending in a multiple birth was especially small in the first two centuries, when it was as low as 0.86 ± 0.3%. Later, the frequency of primi-pluriparae increased to 1.30 ± 0.4%. However, the difference is statistically not significant.

In the first two centuries, the chance of a twin delivery rose to the group of the 11th to 15th conception; in the 18th century the chance increased to the group of the 6th to 10th conception only; and, since the year 1800, the chances of a twin delivery stopped rising after the fifth confinement. Throughout the 437 years under study, there were no twins resulting from the 16th to the 23rd conception.

TABLE 4. RULING FAMILIES; ORDER OF BIRTHS IN TWINS.

Order of births	16th and 17th centuries			18th century			19th and 20th centuries		
	all families†	twin families†	twin births*	all families†	twin families†	twin births*	all families†	twin families†	twin births*
I	18	11	6.5	20	12	14	21	21	17
II-V	48	42	52	52	46	50	54	62	80
VI-X	27	35	32	22	35	30	20.5	15	3
XI-..	7	12	9.2	5.5	7.5	5.5	4.5	2	—
all	100	100	100	100	100	100	100	100	100

† order of all births
* order of twin births, regardless of all other births.

The closer we come to the present, the smaller becomes the frequency of twins (per 100 deliveries). In the first two centuries, one pair of twins appeared per 89 deliveries.[8] In the 18th century, that proportion changed to 1 : 103[9] and since then to 1 : 123.[10] These changes are sur-

[7] Born between 1500 and 1936.
[8] 4,511 singletons and 54 pairs of twins.
[9] 1,826 singletons and 18 pairs of twins.
[10] 1,822 singletons and 15 pairs of twins.

prisingly large if compared with the experience in the general population. Of course, the knowledge about the proportion in the general population extends further than 100 years back only in rare instances. Besides, one ought to realize that in the general population, birth decline as a rule started not earlier than in the third or fourth quarter of the 19th century, while in our sample birth control started in the 18th century. Observers who a few decades ago had analyzed the frequency of twins were led astray by the official statistics and concluded that the proportion of twins to singletons in each country is subject to small annual oscillations only. That this is not so was shown by Prinzing who, in 1931, computed data on millions of births for various countries for three periods, one prior to 1870, the second for 1871-1880 and the third for 1901-1910. In these three periods the proportion changed from 1 : 83 to 1 : 86 and then to 1 : 92. The changes are small, but they show a definite trend in the same direction as disclosed in our study for ruling families. Although the trend is the same, the data collected in Western, Central and Northern Europe and in the U. S. A. demonstrate a much higher frequency of twins than that found in this paper for the ruling families since 1800. However, the proportion of 1 : 123 is by no means extreme. In Greulich's study, Greece is represented by 1 : 131, and Japan as well as several Central and South American countries have a still smaller frequency of twins. One may be skeptical as to the validity of the statistics of most of these countries, but doubts would not be justified with respect to the recording of births in the ruling families for the time since 1800.

The probability of multiple births from young women is small, and in the earliest period of this study it was even smaller than in the last one or two centuries. The same is true for all first conceptions, regardless of the mother's age. Thus, women who married in 1500-1699 and became primi-pluriparae, were 28.0 years of age [11] on the average, while the corresponding value for those who married since 1700 is 23.3 years.[12] Considering the wedding age, as demonstrated in part A (General Mortality of Women), Table 1, of this series of studies, an average age of 28 years for primiparae is rather high. On the other hand, women with a multiple birth between the eighth to fifteenth conception were relatively young. In the first two centuries, these women were 33.7 years of age [13]

[11] 17, 23, 26, 29, 34 and 39 years of age; one case of unknown age.

[12] Once 20, 22, 24, 25 and 33 years, twice 23 years, and three times 21 years of age.

[13] Once 26, 27, 30 and 42 years; twice 32, 33, 34 and 37 years; three times 36 years of age.

and had an average of 10.5 deliveries, and since the year 1700, the corresponding data was 33.3 years and 9.7 deliveries.[14]

Mortality of Twins

In his paper presented to the Royal Society in 1788, Clarke said: "Near one half more twins die, and near one third more are stillborn than of single born children, and why? It is not because they meet with greater difficulties in birth. On the contrary, it is a known fact that being much smaller than other children, women bring them forth with more ease." Clarke believed the twins to die of inanition prior to delivery and of weakness following it. He did not produce any measurements of twins to prove his point, although in maternity wards measuring already had been introduced by I. G. Roederer (1753, (26)).[15] Table 5 demonstrates the differences in perinatal mortality[16] between singletons and twins in Clarke's material as well as in two later periods, one in the 19th century (after Collins) and the other in the 20th century (after Orel (27)).

TABLE 5. PERINATAL DEATHS IN HOSPITALS; 18TH, 19TH AND 20TH CENTURIES.

	The Dublin Lying In Hospital				Vienna University Hospital	
	Years 1754–1784 singletons	twins	Years 1826–1833 singletons	twins	1915–1921 singletons	1912–1923 twins
Number of individuals.....	19,455	662	16,174	480	43,468	1,606
Among them: stillborn.....	953	49	1,063	58	2,000	120
in %.....	4.9	7.4	6.6	12.1	4.6	7.5
died in 1 week...	2,903	207	257	32	3,695	349
in %.....	14.9	31.3	1.6	7.6	8.5	21.7
Total perinatal mortality.....	19.8	38.7	8.2	19.7	13.1	29.2

In part C of these studies (Infancy and Childhood), the danger of wrong conclusions by studying either stillborn or postnatal deaths alone has been discussed. The figures of the Dublin Hospital for the two time periods demonstrate this danger. Even in the same hospital the classifica-

[14] Once 32, and twice 34 years of age.

[15] Initiating measurements in maternity wards, Roederer disproved the general belief that newborns weigh 12 to 16 lbs. on the average. In his book I did not find measurements of twins separated from the other newborns.

[16] Perinatal mortality = ante, intra- and postnatal mortality, that is stillborn plus neonatal deaths in the first 7 days.

tion of deaths in stillborn and neonatal deaths changes, and makes necessary pooling together of pre- intra- and postnatal deaths under the heading perinatal mortality.

For both the singletons and twins as well, the perinatal mortality of the hospital population in Dublin of 1826-1833 was about half that of 60 years earlier, and in both periods the perinatal death toll of twins was about twice that of single born children. Similar is the relationship in Vienna's hospital about the time of the First World War. The comparison of the three sets of figures yields a rather astonishing result. In spite of the great progress of medicine in the 19th century, the perinatal mortality of singletons as well as of twins in Vienna's university hospitals is higher than it was approximately 90 years earlier in Dublin's Lying In Hospital.

In the ruling families, the difference in perinatal mortality between singletons (7.6%) and twins (31.0%) always was larger than shown in Table 5 or than at present in the U. S. A.[17] In the 16th and 17th centuries, the difference was about twice as large; later it diminished. According to Table 6, the perinatal mortality of singletons dropped from 9.6 to 3.5%, while for twins the corresponding values were 38.9 and 10.0%.

TABLE 6. RULING FAMILIES; PERINATAL MORTALITY.

	All newborns	Stillborn and neonatal deaths number	in %
1. Single born:			
16th and 17th centuries	4,511	431	9.6
18th century	1,826	131	7.2
19th and 20th** centuries	1,955	68	3.5
	8,292	630	7.6
2. Twins:			
16th and 17th centuries	108	42	38.9
18th century	36	9	25.0
19th and 20th** centuries	30	3	10.0
	174	54	31.0

** marriages up to 1930.

In later periods of life, in infancy and childhood, twins never had an excess mortality as high as in the perinatal period (see Tables 6 and 7). In the first two centuries, of the survivors of the first week, 15.4%

[17] Yerushalmy and Sheerar found for N. Y. State, 1936 the perinatal mortality of twins (: 16.8%) to be about 2.5 times that of singletons.

(singletons) and 27.3% (twins) died in the first year of life, the difference being about 1:2. The corresponding figures for the time since 1700 were 7.9 and 5.5%, respectively. Here, the excess mortality of twins disappeared entirely. In the 16th and 17th centuries, 78% of all singletons and 50% of all twins survived the first year of life; for the time since 1800 the corresponding values were 93.5 and 89.3%, respectively. Progress in saving life was more evident with regard to twins than with respect to single born children. The same applies to children 1-5 years of age.

TABLE 7. RULING FAMILIES; CHILDREN BORN ALIVE.

MORTALITY OF THE FIRST 5 YEARS OF LIFE.

	Marriages			Marriages		
	1500–1699	1700–99	1800–..	1500–1699	1700–99	1800–..
	Single born			Twins		
1. Born alive.....	4,414	1,774	1,924	96	33	28
died in first year.....	963	272	126	48	7	3
in %.....	21.8	15.3	6.5	50.0	21.2	10.7
2. Survivors of first week.	4,078	1,695	1,887	66	27	27
of them died in first year	627	193	89	18	1	2
in %.....	15.4	11.4	4.7	27.3	5.5	
3. Survivors of first year..	3,451	1,502	1,798	48	26	25
of them died in II-V year	348	199	78	12	4	2
in %.....	10.1	13.2	4.3	25.0	11.7	
4. Survivors of fifth year.	3,103	1,303	1,720	36	22	23
in % of all born alive..	70.3	73.4	89.4	37.5	66.6	82.1
in % of survivors of first week.....	76.1	76.9	91.1	54.6	81.1	85.2

In general, not much is known about mortality of twins who survived infancy. Newman says "their life expectancy is probably as good as that of other children." So far the clubs of twins did not contribute to our knowledge of that issue.

In the first two centuries, twins of the ruling families continued to exhibit a considerable excess mortality in the second to fifth year of life (25.0 ± 6.2 versus $10.0 \pm 0.5\%$). Since 1700, however, the surplus mortality of 1-5 years old twins has shrunk considerably ($11.7 \pm 4.5\%$ deaths for twins versus $8.4 \pm 5\%$ for singletons). At the end of the fifth year, the percentage of survivors increased from 70 to 73 and to 89% in singletons, and from 37.5 to 67 and to 82% in twins (see Table

7). Thus the corresponding figures came nearer and nearer to each other, and since 1800 in the ruling families it has made little difference for the survival of a child whether he entered the world as a singleton or a twin.

At the age of 5-15 years of life, the decade of the lowest mortality, twins never were more endangered than were singletons. Those twins which lacked sufficient resistance to the environmental conditions had succumbed at an earlier age. Both singletons and twins profited from the improvement of living conditions, and during the last 137 years had a lower mortality than before (Table 8).

TABLE 8. RULING FAMILIES; MORTALITY IN LATER CHILDHOOD.

	Marriages			Marriages		
	1500–1699	1700–99	1800–..	1500–1699	1700–99	1800–..
	Single born			Twins		
1. Survivors of the 5th year	3,103	1,303	1,598*	36	22	22*
died in 6th–15th year..	193	99	59	2	2	—
in %.....	6.1	7.4	3.8	5.5	4.8	
2. Survivors of the 15th year	2,910	1,204	1,539	34	20	22
in % of all born alive	65.9	67.9	86.1†	35.4	71.2**	
in % of all newborns	64.5	65.9	84.9††	31.4	55.5	78.6
		75.4%			65.6***	

* born up to the year 1921.
** here were counted only 33 + 26 children born alive, as two were born in 1924.
*** here were counted 64 twin individuals.
† here were counted 1,780 children born alive.
†† here were counted 1,811 children born alive.

At the end of the fifteenth year of life, the percentage of survivors in singletons increased from 66% to 68% and then to 86% and in twins from 35% to 61% and then to 85%. Combining the figures for all children born alive since 1700, we find the survival ratio for singletons to be 76.9, and for twins 71.2%.

Mortality of Twins in Relation to That of Their Siblings

In the ruling families, the perinatal mortality of singletons in families without twins was a little lower than in families with twins. In the first three centuries, of 5,879 singletons who had no twin siblings 508, or $8.6 \pm 0.4\%$ succumbed in the perinatal period, the corresponding figures for singletons who had twin siblings were at the same time 458 and 54,

or 11.8 ± 1.5%. The difference in mortality is not significant and becomes still smaller if the rest of the first year of life be included in the calculation (20.7 and 21.8% respectively).

There is a high correlation between the perinatal mortality of singletons and their twin siblings. In families without perinatal mortality of their singletons, twins run a lower risk of dying during the perinatal period than was the risk for twins in families in which a certain number of singletons were either stillborn or died within the first week after birth. In the former group of families, consisting of 46 units, 16 had lost either one or both twins in the perinatal period, while in the latter group of families the corresponding two figures were 31 and 17 families. In the former group 22.4± 4.2% and in the latter group 48.5 ± 6.1% of the twins died in the perinatal period, the difference being statistically significant.

TABLE 9. RULING FAMILIES; MORTALITY OF TWINS IN FAMILIES.†

	A/with	B/without
	perinatal mortality of their single born children	
1. Number of families (mothers)	31	46
Number of twins (individuals)	66	98
Number of individuals who died in perinatal period	32 = 48.5 ± 6.1%	22 = 22.4 ± 4.2%
2. Number of survivors	34	76
of them died before end of infancy	9 = 26.5%	11 = 14.5%
3. Perinatal and infant mortality	41 = 62.1%	33 = 33.7%
4. Survivors of infancy	25	65
of them died in 2nd–15th year	3 = 12.0%	12 = 18.4%
5. Survivors of 15th year	22	53
in % of all born twins	33.3 ± 5.8%	54.1 ± 5.0%

† Five families with twins but without singletons are not counted here. Of the 10 children only one died.

The difference in the perinatal mortality as shown in Table 9 is of interest on account of recent studies on so-called erythroblastosis of infants in connection with the Rh factor. This factor might have been involved in some of the cases. However, according to H. A. Schwartz and P. Levine (28) erythroblastosis is present in 4% to a possible 8% only of the perinatal deaths. There is no reason to believe that isoagglutination due to hereditary factors was more frequent in former centuries. Thus, though the Rh factor might have contributed to the increased perinatal mortality in the A group of twin families, its importance should not be over-

estimated. Skepticism is indicated also on account of the huge difference in the infant mortality [18] past the neonatal period. Although agglutination, haemolysis and anemia due to the Rh factor may kill the infant also later, usually death occurs about the time of birth. It is therefore probable that other factors, such as diseases of parents and prenatal as well as infant care were responsible for the differences shown in Table 9.

The excess mortality in the twins of the A group of families is a phenomenon limited to the first year of life. Later, the survivors have a rather lower mortality than twins of the B group. Nevertheless, at the end of the 15th year there is still a statistically significant difference in the survival ratios of the two groups. Of the twins whose single born siblings did not die at all during the perinatal period, $54.1 \pm 5.0\%$ survived childhood (= 15 years of life), the corresponding figures for the other group of twins being $33.3 \pm 5.8\%$.

In Table 9 there are not mentioned five pairs of twins who did not have singleton siblings. Of these ten twins only one died, and nine lived to be 15 years old and older. Adding these five pairs of twins to the group B of twin families would still increase the differences in mortality and survival rates correlated with the perinatal mortality in the respective families.

Discussions

During the 437 years under study, the perinatal mortality of twins underwent a substantial reduction. Since 1800, perinatal mortality is about ¼ of that in the first 200 years. This strong reduction had no antiselective effects upon the surviving twins. The improvement in perinatal mortality of twins partly may have been due to improved physical conditions of the mothers. In recent centuries, young women seem more fit for reproduction than they were in more remote times. The primipluriparae became younger, the interval between marriage of women below 25 years of age and the time of the first delivery resulting in twins shrank from 4.3 years to 2.0 years. It is difficult to explain this change in definite terms, as long as the genesis of twins in general is not based on a more solid scientific basis. Apparently either the ovulation process in young persons became more abundant or the stage satisfactory for the simultaneous gestation of a second embryo is now being earlier reached by the uterus than it was in the more distant past. It is known that one of the twin embryos may die in the first weeks and may be entirely overlooked at the time of the delivery of the other embryo. If on account of a higher

[18] Between A and B in Table 9.

frequency of infantile uteri in former centuries one twin embryo more frequently succumbed at an early stage of development, then the discussed changes would be the natural consequence.

With regard to twins, constitution, heredity, nationality, race, geography, maternal age and order of births have been investigated. Our study suggests that also social conditions should be considered. When unfavorable living conditions prevail—either on account of the economic status or of customs—twins appear to be rare in the age of incipient and most intensive reproductive activity. With improved conditions, twins appear more frequent in these younger age groups and by this the total ratio of twins increases, too. That increase finds its end when birth control has considerably reduced reproductive activity in higher age groups. In part A of this series (pages 438-439) customs have been referred to, responsible for high mortality of young women (15-24 years of age) in former centuries. The same customs apparently kept the twin ratio low in young women. Later, with the change in customs the bodily status of young women improved enough to raise the ratio of twins to all births, but at the same time birth control—in ruling families practised for 200 years—caused a decline of the frequency of twins in higher age groups, thus reducing the total ratio of twins. Perhaps a part of the differences in twin ratios between Greece and Japan and other countries is due to social conditions which do influence the twin ratio in all or at least in the younger age groups.

Another item is worth mentioning. Infants of ruling families, as a group always have enjoyed the best care available. Consequently one would expect a uniformly reduced perinatal mortality. Yet, in these families the differential between the mortality of twins and singletons is larger than in the general population. In part C of this series we have shown that the methods of care successful in infancy, influenced but little the perinatal period. It is only in the last few years that also in this respect some progress has been made.

We may be more successful in preventing a premature birth of singletons than of twins. If this is so, in countries with developed maternal care, the difference between perinatal mortality rates of twins and of singletons should be higher than in countries with a poor antenatal care.

Summary and Conclusions

1. Hypotheses as to the genesis of twins and their familial occurrence are shortly reviewed. Social conditions should be included in the complex of factors involved in the ratio twins: singletons of a population.

2. The Hellin-Zeleny rule concerning the numerical relationship between singletons, twins, triplets, quadruplets, quintuplets and sextuplets is historically analyzed. That rule is supplemented here by a rule concerning *mothers* of multiple births and mothers having more than one set of multiple births of equal or different litter size. The relative frequency of various combinations is shown, derived from finding that a mother with a second pair of twins is about as frequent among all women who had twins as are these women among all who had born. The new rule permits the development of a scheme embracing more interrelationships than did the Hellin-Zeleny rule.

3. In the general population, the frequency of twins is diminishing; the changes are small. In the ruling families, in the 16th to 18th centuries, the frequency of twins corresponded to that exhibited by the general population in recent times. Since 1700, in ruling families the frequency of twins in relation to all deliveries dropped considerably. These changes are due to the birth decline, and due to the changed age distribution of mothers.

4. In the medical literature high fertility of mothers of twins has been stressed repeatedly. In the ruling families, such mothers had a surplus fertility (of 3 to 3.5 children) in the 16th to 18th centuries only. Later, the excess fertility as compared with mothers without twins shrank almost to the point of disappearance.

5. In ruling families of the 16th and 17th centuries, perinatal mortality of twins was four times that of singletons. Later, the perinatal mortality of twins declined more extensively than that of singletons, so that the proportion changed to 3 : 1. In the general population perinatal mortality of twins as well as of singletons is higher and the proportion of both to each other is as 2 : 1 to 2.5 : 1.

6. Twins who survived the perinatal period have an excess mortality also in the five following years of life, but no excess in later childhood.

7. In the 16th and 17th centuries, 64% of singletons survived childhood (15th year of life) while only 31% of twins survived. Since 1800, the corresponding figures in ruling families are 85% and 79% respectively; they are close to each other.

8. There is a high positive correlation between the perinatal and infant mortality of twins and the perinatal mortality of their singleton siblings.

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CERTIFYING SURGEONS—EXAMINING SURGEONS, A CENTURY OF ACTIVITY

(Great Britain 1844–1944)

LUDWIG TELEKY

The "Health and Morals of Apprentices Act 1802" was the first labor-protection act in the factory age. The "Visitors" who were to take care of the execution of the law proved to be entirely insufficient, and so the Factory Act of 1833 ordered factory inspectors to be appointed. Their chief task was to put into practice the law prohibiting the employment in textile factories of children under 9 years and allowing the employment of children from 9 to 13 years only on the basis of a physician's certificate as to their physical fitness. Rickards, the inspector of Manchester, divided this district in 5 parts and appointed for each of them a physician who had to grant the certificates as "Certifying Factory Surgeon." But the Home Secretary denied the inspector's right to do this. In their reports the 4 inspectors again and again emphasized the impossibility of getting honest, reliable certificates and claimed the right to appoint certifying surgeons and to deny to any other person the right to give such certificates.

Finally the Factory Act of 1844 granted the factory inspectors the power to appoint such "Certifying Surgeons," who, besides the right of making out such certificates had "to investigate and report on accidents occurring in any factory for which they had been appointed to grant certificates of age." The Government prescribed the forms for these certificates as well as the fees which the manufacturer had to pay, who, however, was allowed to deduct part of them from the child's wages. Agreements between the physician and the manufacturer concerning the fees were permitted.

Originally the inspector had to appoint the certifying surgeon of his district, but later on, after the organization of factory inspection (1878), the chief inspector of factories and workshops was given this right, and he practises it now by a public announcement of the vacancy in the medical journals and by consulting the senior medical inspector (appointed 1898).

In districts where there is no certifying surgeon the poor-law medical officer may act in this capacity. The Secretary of State may also give the

right of acting as certifying surgeon for a certain factory to a medical practitioner engaged by the owner of that factory for the medical supervision of persons employed by him.

After the introduction by law of birth registers (England 1837, Scotland 1854) some people were of the opinion that certifying surgeons might be superfluous, but Inspector Robert Backer (1858-1878) showed that many birth-certificates were falsified and that some of the certifying surgeons rejected many children by reason of bad health as well as age. Therefore the certifying surgeons were retained in this part of their activity and are still today. Of course, their activity has been changed in various respects. The age for work in factories (not textile mills only) has been raised to 14 years; for young persons from 14 to 16 years of age the certifying surgeons' certificates of fitness are necessary. Most important is the fact that the certifying surgeons were given the right (1901) to issue certificates qualified by conditions as to the work on which the young person is fit to be employed. Some minor changes in the certification and the certificates cannot be discussed here. In the Factory Act of 1937 the title of the " Certifying Surgeons " was changed to " Examining Surgeons " owing to the many other tasks they had to fulfill besides certifying.

The fees of the Examining Surgeon were fixed by Order in 1938 in the following way, subject however to agreements between the surgeon and the employer: Examination of young persons, 5 sh. for the first person and 2 sh. for each other person examined on the same occasion. For examination in dangerous trades (see later), 2 sh. 6 d. for the first, 1 sh. for each other person; besides for the trip a fee of 1 sh. for each mile has to be paid, if the factory is more than two miles from the physician's residence. The fees for examination in Workmen's Compensation cases are higher.

In 1939, the last year in which statistics were published, the examining surgeons examined 406,575 young persons, of whom 5,681 were rejected, 4,204 got certificates under the condition of a re-examination, 8,988 under certain conditions pertaining to the nature of their work. 2,510 certificates were given provisionally pending the results of advice or the receipt of school health records.

Among the causes of rejection were these: Pediculosis 2,233, Diseases of the Eyes and Eyelids, 1,409, Diseases of the Skin 445, Diseases of the Circulatory System 266, Diseases of Ear, Nose and Throat 223, etc.

To make out certificates for young persons was not and is not the only task of the certifying surgeon. The Act of 1844 had given him also that

of investigating accidents. But concerning accidents produced by mechanical causes, such investigations became the more difficult for a physician, as machines became of a different kind and more complicated. The Police Factories Act of 1916 abolished the investigations of accidents by the certifying surgeon who, however, should continue to investigate and report 1) upon cases of injury caused by exposure in a factory to gas, fumes or other noxious substances or due to any other of the causes specified in the instructions of the Secretary of State; 2) upon cases referred to him by the factory inspector in pursuance of those instructions, and 3) upon all cases of occupational diseases notified by a practitioner. For all these purposes the certifying surgeons have the same power as a factory inspector. He is remunerated for each separate case by the Secretary of State.

After occupational diseases had attracted greater attention in England the Factory and Workshop Act of 1895 prescribed that the medical practitioner attending a patient " whom he believes to be suffering from lead, phosphorus, arsenical or mercurial poisoning or anthrax contracted in any factory or workshop " should send a notice to the Chief Inspector of Factories. The latter gives the notice to the local factory inspector and certifying surgeon, whom the manufacturer also is obliged to inform. In 1915 this list of notifiable illnesses was extended by the Secretary of State to toxic jaundice (that is jaundice due to tetrachlorethane or nitro- or amido-derivatives of benzene or other poisonous substances), in 1919 to epitheliomatous ulcerations due to tar, pitch, bitumen, mineral oil or parafin etc. and to chrome ulcerations, in 1925 to poisonings by carbon disulfide, aniline, in 1936 to manganese. For his notice the practitioner receives 2 sh. 6 d. from the Secretary of State. If he fails to send the notice he is fined up to 40 sh.

When notification was introduced (1896) 1050 cases were notified (and therefore investigated by the certifying surgeons), among them 1030 lead poisonings. The greatest figure was reached in 1898 with 1,327 reported cases. In 1939 although so many more illnesses had been indicated as subject to notification, only 506 notices were made, among them 109 lead poisonings, epitheliomatous ulcerations by tar products (160 cases) and chrome ulcerations (159 cases).

The number of cases has changed and—as we see—their natures too.

In some dangerous trades, periodical examinations of the workers are prescribed by permanent orders of the Secretary of the State. They mostly concern workers endangered by lead (11 different trades), by carbon disulfide and nitro- and amido-derivatives of benzol and its homologue, or

chromates (2 trades). It is to be regretted that since the resignation of the famous Senior Medical Inspector, Sir Th. Legge (1926), no new such prescriptions have been ordered.

The examination has to be performed, according to the danger involved in the work, in weekly, semi-monthly, monthly or quarterly intervals by the certifying surgeon, and in some cases by an "appointed surgeon" (approved by the Secretary of State). There were 341,138 such examinations in 1938. 176 persons were rejected in the first examination, 1,057 suspended. Besides that, 32,036 voluntary examinations were carried out with 52 suspensions. For this examination the certifying surgeon has to be paid by the employer (see above).

As a matter of fact the certifying surgeon, occupied with all these investigations and examinations, acquired at least in industrial districts a vast knowledge of occupational diseases. It is, therefore, understandable that this knowledge was made use of when those industrial diseases which had been notifiable since 1895, were included in the Workmen's Comp. Act (1906). Compensation is given only if the certifying surgeon certifies that the workman is suffering from one of these diseases and is thereby disabled from earning full wages through the work at which he was employed. Therefore the first step which the worker has to do, if he wishes to get compensation, is to see the certifying surgeon, who often has already received the notice from the attending physician or the employer, and who very often knows the factory and has the right to make investigations.

In such a way a guarantee is given that every claimant is examined very soon after the beginning of his illness by an impartial physician, experienced in the field and having every right to investigations. If the employer or the worker are dissatisfied with the certificate of the certifying surgeon or the refusal of such a certificate, they have the right to appeal to a "Medical Referee" who is appointed by the Secretary of State. His certificate is conclusive, as is that of the certifying surgeon in case no appeal is made and as far as it is kept within the limits of his statutory contents i. e. concerning medical and hygienic questions.

The Trade Unions have some complaints against the institution of medical referees. First they wish specialists to be appointed. That wish has been complied with, at least, partially, e. g. by the appointment of eye specialists. Furthermore they wished the individual referee to be replaced by a Board, as it is used in questions of silicosis and asbestosis which are treated by special regulations (not discussed here) differing from those concerning other occupational diseases. In the course of time

the schedule of compensable industrial diseases, comprising only five in the beginning, has been much increased and now embraces 35 different illnesses.

The following figures from the year 1938 give an insight into the extent of the activity of the certifying surgeons in this field: 11,081 cases of disablement caused by one of these diseases were compensated for the first time, and 33 cases of death were compensated.

It may finally be mentioned that every year the certifying surgeon makes a report about his activity to the Secretary of State.

In England and Scotland there are about 1800 certifying surgeons. In 1926 Th. Legge explained that the number of "appointed surgeons" is very small, and that it would be better to replace them entirely by certifying surgeons. He added that of the certifying surgeons only about 150 to 200 had much to do, as they were active in the most important industrial districts.

This number is likely to have increased in the meantime. At any rate it is certain that a much larger number have acquired a good experience in their field. It is natural, indeed, that certifying surgeons in districts with very little industry should lack experience, their activity being of no great importance. But the fact that every case of occupational disease in the district come to the knowledge of this single physician gives him a certain experience even in a place where industry is scarcely developed.

The work of the certifying surgeons is highly appreciated by those who have the best insight into their activity, i. e. the medical inspectors who have always to work in close connection with them. The Senior Medical Inspector, Sir Th. Legge, wrote in 1926:

> Had it not been for the existence of these clinical observers distributed throughout the country the number of medical inspectors would naturally have had to be greatly increased. Their services in the protection of child labor and the investigation of notifiable industrial diseases have been of enormous value, but like all old institutions, their power should now be overhauled to make them still more useful by extension. I would insist that it is preventive medicine on the clinical side that is wanted in the factory and not the administrative officer.

Legge's successor J. C. Bridge writes in his 1938 report that he has to thank the Association of Certifying Factory Surgeons for their useful cooperation in the introduction of the Factory Act of 1937.

It is very difficult to get statistical data pertaining to the efficiency of the certifying surgeons alone. But there are some such data showing how highly efficient the entire English system is in a field in which the certifying surgeons cooperating with others play an important role:

The number of:	1900	1939
Lead poisoning	1058	109
White and red lead work	377	10
Paints in different industries	50	2
Pottery	210	7
Electrical accumulator work	33	4
Paints in different industries	50	2
Arsenical poisonings	22	4

In its fight against occupational diseases the English system obtains these excellent results chiefly by the following measures:

Exact regulation for the different dangerous industries.

In these regulations: *periodic medical examinations* by impartial physicians, *appointed by the State* or, at least, approved of by the State.

Such examinations, first introduced by English legislation a hundred years ago, have gradually been adopted by other countries.

In the Netherlands the examinations of young persons and periodic examinations are performed by the medical inspectors of the factories.

In Germany, where periodic examinations have been compulsory in some dangerous trades for many decades, the employer had in most of the cases free choice of the physician. But that changed, and now the appointment or the dismissal of these physicians must have the approval of the medical factory inspector.

In the *compensation* of occupational diseases, the existence of such impartial physicians who are experienced in this field made it possible to solve the most difficult problem: the achievement of a correct diagnosis.

The diagnosis of most of these diseases (one exception is silicosis) is possible only if an experienced physician had seen the patient in the first days of the illness.

It is therefore necessary that the worker who claims to suffer from an occupational disease should be seen as soon as possible by such a physician. But where are such physicians to be found?

The statistics of occupational diseases show how rare the opportunities are for the practitioner to acquire such an experience! Experienced physicians can be trained only by making the small amount of material come to the attention of a small number of physicians. "Occupational diseases" are a special field of medicine as are the diseases of the ear or of the eyes, etc.—but a wider one.

The English system, with its certifying surgeons who have to give the first certificates for the claimant, has solved this problem in an excellent way.

Germany's first regulations ordered that a man who pretended to suffer from an occupational disease should be examined as soon as possible by a "proper physician," approved by the medical inspector of the factory. The newest regulation orders an examination to be made by the medical inspector of factories or a physician delegated by him.

Certainly, as there are only few medical inspectors in most of the countries, they would be taken from their principle work, if they were to do the entire work for compensation of occupational diseases, but they are the predestined experts for the higher courts.

So the English system of "Certifying Surgeons" seems to be the ideal solution for the two problems, viz. the fight against occupational diseases and their compensation.

CONTEMPORARY TENDENCIES IN THE HISTORY OF MALARIOLOGY*

SAUL JARCHO

A large proportion of all historical writing and study is based on the conception that history consists merely of the description or narration of past events. Broader than this type of *laudatio temporis acti* is the attitude of those more practical historians who would employ the study of the past as an instrument for analysis of the present. According to a still broader concept history is the study of processes, including processes which are not extinct but which extend from the past through the present into the undiscovered bourne of the future. It is with this attitude that the present study has been undertaken. The author proposes (1) to assemble for examination the history of malariology in the recent past, (2) to identify the principal trends of the present, and (3) to consider what developments can be expected in the immediate future.

In estimating these trends and developments the historian of malariology is justified in making a basic assumption. He may be permitted to assume that the ultimate objective of malariology is the eradication of the disease or at least its reduction to a degree such that important economic or social damage is no longer produced. This assumption provides a method whereby trends can be evaluated. It becomes possible in this way to select those trends of research which lead toward the eradication of the disease and to distinguish them from other trends which lead in other directions. The scope of this essay affords no room for teleological discussion. While leaving out of account the question of whether or not *all* studies in malariology are purposefully aimed at the eradication of the disease, we may nevertheless find it useful to observe which studies recognizably advance toward that result.

Research in malariology divides itself into several categories: (a) studies of vectors, (b) studies of plasmodia, and (c) studies of the host. In the last-named of these categories only the problem of host-parasite relations will be considered in the present essay. Such important subjects as clinical malariology and the epidemiology and sociology of malaria will be reserved for separate treatment in a work of larger compass.

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Sixty-four years have elapsed since Laveran initiated the scientific study of malaria. The causative plasmodia are now known in great detail. The methods of transmission and many vector species are likewise known in detail. Drugs are available which restrain or impair the multiplication of the plasmodia but which cannot eliminate them in the sense of a *therapia magna sterilisans*. No true causal prophylactic drug has been found. With knowledge now extant the disease has been eradicated from small areas. Eradication from large areas, or continents, or from the whole world is theoretically possible but socially impossible. In other words, although sufficient technical knowledge is now in existence there are obstacles to its utilization and the disease continues to prevail widely.[1] There is no evidence to indicate that the total quantity of malaria in the world is appreciably less than at any time in the historical past. In a few areas, such as England and parts of the United States, the disease has regressed. This however is not the result of a planned attack but is the fortunate collateral or incidental consequence of such circumstances as urbanization or changes in agriculture. In the United States, a commonwealth not deficient in human or financial resources, approximately one-seventh of the national domain is malarious. In a few unblessed countries the disease flares forth violently from time to time. One such outbreak in Ceylon destroyed 80,000 lives in the space of seven months.[2] In most countries within the temperate and tropical zones the malaria map shows large patches representing endemicity and occasional specks representing areas of control or experimentation.[3,4,5]

The last few years have witnessed the extension of the disease to thousands of men under arms. Since the return of these men to their homes will afford additional opportunity for dissemination of plasmodia, it is inevitable that local outbreaks of malaria will occur. Whether large general outbreaks or persistent endemic foci will come into being can hardly be predicted. When military operations cease and armies are withdrawn, malaria control will fall into desuetude in demilitarized districts. Such places might be made to yield valuable information about the epidemiological vagaries of the disease. The same is true of districts in Albania and other countries where control works constructed by engineers have been subjected to bombardment.

After these brief introductory comments we may now proceed to examine several principal aspects in greater detail.

In the old science of entomology the oldest and best developed department is that of taxonomy. The discovery of the sporogonous cycle of the plasmodium inevitably intensified the quest for new mosquito species.

As these species multiplied and filled the literature, increasingly complex taxonomic systems became necessary. A significant example of this process is seen in a recent systematic treatise in which anopheline mosquitoes are arranged not merely according to genera and species but according to genera, subgenera, groups, series, and species.

In this connection one may speculate on the probability of new species being discovered. If all the known vector species are listed in chronological order it is easy to construct a graph in which years are represented as abscissae and numbers of known vector species are represented as ordinates. Such a graph represents the gradual increase in the number of known vector species. The curve shows a steep grade for the years 1818 to 1828 and a second and steeper ascent for the years 1899 to 1906. The second of these grades represents vectors which were discovered in the early years after the disclosure of the sporogonous cycle. The graph taken as a whole does not conform to any recognizable mathematical type. Quite evidently the discovery of new vectors does not take place at anything like a constant rate. Instead it becomes apparent that discoveries of vectors have occurred during brief periods of intense scientific activity. Since no regular rate can be recognized there is no evidence to indicate that the pace of discovery is now increasing or decreasing and no inference can be drawn as to the probability of new species being discovered. At the present juncture there is abundant opportunity for military entomologists to lengthen the list of known vectors. The establishment of new air routes and new airplane bases may lead to the same result. Further research should likewise eventuate in the recognition of new subspecies or varieties.[6] Thus the morphological diversity of species such as *Anopheles gambiae* may require finer classification.[7] It is also to be expected that species already described will gain or lose in importance as vectors. Such has been the case with *A. bellator* in Trinidad. This mosquito had been under the observation of F. W. Urich as early as 1900,[8,9,10] at which period it was a forest dweller. Between 1895 and 1905 large areas of forest were cleared to make room for the cocoa plant and its shade tree, the immortelle. *A. bellator* has been able to thrive in the bromeliads which densely colonized the immortelles and has now become the principal vector of malaria in the inland cocoa-growing districts of Trinidad. In these districts it has infected American soldiers.[11,12,13]

The attack on *A. gambiae* in Brazil[14] is famous as the first instance of the total purposeful extinction of a mosquito species from a continent. Several aspects of the campaign are of interest to the historian. Because of its vast scope and great cost the enterprise could scarcely have been

conducted by private individuals. Conceivably it might have been executed either by one of the great charitable foundations or by a government. Actually the work was done by the Rockefeller Foundation and the government of Brazil acting in concert. At other times and in other parts of the world the control of malaria has been undertaken by many different types of organization—governmental, commercial, industrial, agricultural, scientific, and charitable. It would be desirable for sociologists to study these diverse examples in order to ascertain which forms of social agency and which types of governmental organization tend to be most successful in the control of malaria, and which characteristics of a social system favor the control of disease in general.

In the control of malaria by "species sanitation" a line of historical continuity is evident. Species sanitation was introduced by Malcolm Watson [15] and has become traditional with the British and the Americans. It has also been studied by the Dutch and the Italians. The French, on the other hand, continue to emphasize quinine prophylaxis. In this respect it is instructive to contrast the section on malaria prevention in Manson-Bahr's text-book [16]—"the basis of malaria prophylaxis is the fact that particular species of mosquitoes are necessary for the propagation of parasites"—with the comparable section in Brumpt's Précis de Parasitologie.[17] Similarly a German author [18] discussing the prophylaxis of malaria in Nazi-occupied Greece says:

> It must be mentioned that we attacked the problem of malaria first of all by means of drug prophylaxis, whereas the English attach greatest value to mosquito control.

The subdivision of the *maculipennis* complex introduced the use of taxonomic criteria based on characteristics of the mosquito egg. Presumably this technique is capable of useful extension to other mosquito species. The characteristics of the pupa continue to be of little taxonomic usefulness.

Most of present-day knowledge of mosquitoes has to do with taxonomy. Knowledge of ecology is as yet limited and tends to be superficial. The metabolism and biochemistry of the mosquito are almost completely unexplored. This is attributable at least in part to the intense specialization which is generally characteristic of entomologists. Entomologists versed in biochemistry are rare and would seem to be concentrated chiefly in the field of economic entomology. At the present time a complex problem is attacked by a team of specialists rather than by a single individual trained in the techniques of several sciences.

The control of mosquitoes by chemical methods has made notable

progress in the very recent past. An interesting feature is the increased use of measures directed against the adult mosquito. Such measures proved their value in the *gambiae* campaign in Brazil[19] and have attained high efficiency through the introduction of the aerosol bomb. Larvicides are being improved *pari passu*, under the stimulus of military necessity.

Although methods of mosquito control steadily improve, there is no warrant for the expectation that world-wide control of malaria will ever be accomplished through extinction of the vectors. The problems of species sanitation are too diverse, control measures are both expensive and impermanent. The reader may imagine how far we would have progressed in the control of smallpox if a separate survey were needed for each district where the disease occurred.

Having reviewed a few salient tendencies in the study of vectors we may now turn to studies of plasmodia.

No valid plasmodia of man have come to light since Stephens' discovery of *Plasmodium ovale*[20] and there is no adequate basis for estimating the probability of further additions to the list. There is no clinical or epidemiological evidence which requires us to assume that new and undescribed plasmodial species may be in existence. Perhaps a few plasmodia of lower animals, especially plasmodia of uncommon and unfamiliar hosts, may still await the discoverer. It is conceivable that rare cases may be found in which human beings have become infected by heterochthonous plasmodia such as *Plasmodium knowlesi*.

Evidence has been adduced to show that at least two of the plasmodial species may be subdivisible into races or strains.[21,22] It can be surmised that such strains or races will be comparatively numerous. The systematic detection of races will require subtler methods than present-day staining and oil-immersion microscopy. Immunological and biochemical techniques may be requisite. Once these improved techniques are developed, the discovery of new races will proceed rapidly at first and then more slowly. The recognition of new races will produce a new subspecific taxonomy. Whatever be the practical usefulness of race taxonomy and race physiology in the remote future, the study of these subjects must be regarded as highly promising for the immediate future.

These considerations suggest that we are near a halting-point in the morphological study of the erythrocytic and the sporogonous cycles of the human plasmodia. Wilson has recently shown that it may be possible to recognize alterations in parasites taken from a partly immune host.[23] Even the bewildering forms encountered in thick-smear preparations have been catalogued and reduced to order.[24,25] Armed with methods of this

kind we are forgetting the old technique of fresh preparations, which Craig in a recent book has properly attempted to recall from obsolescence.[26]

The abandonment of simple methods and their attempted resurrection is perhaps a characteristic of sciences which have passed beyond their earliest stages. But although a simple technique such as the fresh-drop preparation may occasionally suggest new lines of thought, its potential intrinsic usefulness as a weapon of discovery would seem to be negligible compared with the potentialities inherent in electronic microscopy, vital staining, and new cultural methods.

A discussion of the plasmodia naturally leads to a consideration of plasmodicides. Although it is evident that Sydenham recognized certain limitations to the efficacy of cinchona, it is only within the present century that the limitations of chemotherapy have come clearly into focus. It is now well established and well known that quinine, atabrine and plasmochin are alike powerless against the sporozoite and hence cannot act as true causal prophylactics. Indeed it has become increasingly obvious that these drugs in their action against intra-erythrocytic parasites merely render such parasites susceptible to attack by the powers of the host. Limitations of this character have been no deterrent to the partisans of chemotherapy. Indeed this field is now being canvassed with unprecedented thoroughness and large groups of chemical compounds are being gathered and subjected to systematic assay.[27] Interesting recent empirical discoveries deal with the action of thiobismol[28] and the unexpected effectiveness of sulfonamides against *P. knowlesi*.[29]

Since all evidence indicates that we are about to witness a period of active research for improved chemical prophylactics it is relevant to consider the possibilities of this trend. What is the maximum benefit that a chemical prophylactic could offer? The best drug which we can imagine at the present time is one that would prevent the development of sporozoites, would have no toxic effects, and would retain its effectiveness over long periods. Such a drug if it also possessed plasmodicidal properties, might conceivably reduce the size of the plasmodial reservoir and thereby greatly restrict the transmission of the disease. Yet although this hypothetical drug would certainly be a boon to armies and other limited groups which can be kept under strict control, in the world at large it would encounter the aforementioned social obstacles which have so greatly curtailed the utilization of the older anti-malarials.

There is moreover one additional consideration which causes the present surge of research in chemoprophylaxis to be regarded with misgiving. The fundamental mechanisms of cure and of relapse in malaria are still

imperfectly understood and there are those who believe that problems of this more profound type should be given priority. The present author feels that the present "chemoprophylactic renaissance" in malariology is attributable to the fame of the sulfonamides and that during the immediate future the attention of research scientists should preferably be directed toward a study of the basic mechanisms of the disease.

In a previous paragraph mention was made of cultural methods. Cultural methods in fact constitute one of the greatest desiderata of contemporary malariology. Their development would immeasurably aid the immunological study of malaria and would also make it possible to study the chemical, physical and biological properties of the plasmodium.

Major lacunae also exist in our understanding of the extra-erythrocytic cycle. Indeed the very existence of such a cycle in the plasmodia of man has recently been contested by a prominent malariologist [30] and the subject is one which beckons to be studied. If, as appears almost certain, the extra-erythrocytic phases occur within the reticulo-endothelial system, fundamental research in the general physiology of that system would lead to important progress in malariology.

Morphological changes in the reticulo-endothelial system represent one of the more accessible aspects of the response of host to parasite. Of even greater potential importance is the study of humoral responses. This part of malariology has hardly begun to develop. Studies have been made of changes in the simpler chemical constituents of the blood serum but these at present appear to offer little. Much more promising are the immunological studies, which have been summarized recently by Coggeshall in an article entitled "Immunity in Malaria." [31] A few quotations will serve to illustrate Coggeshall's present views:

> Some of the perplexities of the malaria problem are concerned with those factors associated with the acquisition and development of ***immunity, a phase of malariology sadly neglected*** (italics not in original text). . . . It was shown . . . in 1937 for the first time that specific protective antibodies could be demonstrated regularly in the serum of rhesus monkeys with chronic *Plasmodium knowlesi* infection . . . (The) demonstration of the passive transfer of immunity has since been confirmed. . . . Accumulated data furnish definite proof of the existence of the humoral factor in malarial immunity. . . . Except for the very unlikely possibility that a new strain of malarial parasite with exceedingly broad antigenic immunizing complexes should be discovered, there is little hope for an effective living vaccine in malaria. The use of inactivated parasites promises no more.

Coggeshall's statements express the opinions and describe the attitude of the active research worker who is concerned with practical problems susceptible to precise formulation and study in the immediate future. The

historian necessarily must have a different outlook since it is his function to place the problem in perspective and to attempt to see into the immediate future and beyond—even if length and breadth of view result in loss of detail. If the problem of immunity in malaria is studied in this way certain aspects become apparent. It is inconceivable that research will stop short when the limits of spontaneous immunity to the plasmodium shall have been defined. The malaria problem will continue to be an urgent one and will continue to demand a solution. It is therefore inevitable that methods will be devised whereby the spontaneous resistance of the host will be increased, and that such methods will succeed one another until successful techniques of immunization are devised. It is impossible to predict whether this will be accomplished by means of a "new strain of malarial parasite with exceedingly broad antigenic complexes" or by the use of inactivated parasites. It is at least equally possible that spontaneously formed antibodies will be purified or synthesized, or that the discovery of a new principle of immunology will lead to the solution of the problem. In any field of knowledge the specific influence exerted by future discoveries can almost never be predicted.

It must be admitted however that any hopes of disease eradication based on scientific immunology must derive their support from general historical considerations rather than from any definite historical precedent. History as yet affords no instance in which a disease of human beings has been eradicated through modern immunological techniques; even the control of smallpox owes little or nothing to the newer immunology. Nevertheless it seems almost inevitable that research in the immunology of malaria will ultimately make the necessary technical advances even if when these shall have been achieved the social obstacles will still remain. All evidence points to immunology as the field which at the present time offers greatest opportunity for fruitful research and greatest hope for the ultimate eradication of the disease.

This conclusion has been well phrased by Rosinger:[32]

> . . . our continuous emphasis on attempts to solve the malaria problem by endless work and discussion on prophylaxis and the comparative efficiency of the different malaria drugs have led us into a *cul-de-sac*. In looking for a way out of it we are using up valuable time and energy, part of which could more profitably be employed in investigating humoral pathology, serology, and the problem of immunity in malaria.

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THE TRANSPLANTATION OF TESTES

ARNOLD ADOLPH BERTHOLD

TRANSLATED BY D. P. QUIRING

Translator's Note

Now and then the account of a basic research appears in the literature. More rarely, it is expressed with such clarity, with such concentration on essentials, that the described problem appears to have solved itself.

Some years ago I had occasion to refer to the short paper of Professor Berthold of Göttingen on the transplantation of the testes in six cockerels. The account was published in the *Archiv für Anatomie, Physiologie und wissenschaftliche Medicin*, pp. 42-46, 1849. Because of its inaccessibility in the original and because it is so frequently overlooked, it was thought worth while to translate the short four and a half page paper, the clearcut conclusions of which have become the foundation of modern endocrinology. Apparently Berthold was the first to indicate that the internal secretory products of the testis were taken up by the blood and thence transferred to the other systems of the body.

Translation

On August 2 last year, I caponized six young cockerels, *a*, *b*, *c*, each three months old, and *d*, *e*, *f*, two months old. Wattles, combs, and spurs were not removed from these animals. Both testes were taken from cockerels *a* and *d*; these animals later showed the characteristics of capons; they were not aggressive, they fought with other cockerels rarely and then in a half-hearted manner, and they developed the monotone voice of the capon. Comb and wattles became pale and developed but slightly; the head remained small. When these animals were killed on December 20, the former site of the testes showed but a small scar. The spermatic cords were recognizable only as delicate fibers.

Cockerels *b* and *e* were castrated in similar manner except that only one testis was removed from the body; the other remained isolated in the body cavity.* In cockerels *c* and *f*, however, both testes were taken from

* Apparently it was separated from its attachments and left lying loosely in the body cavity. (Translator's note.)

the body; one testis of cockerel *c* was placed in the body cavity of cockerel *f*, and one from *f* was placed in the body cavity of *c*, among the intestines.

These four cockerels (*b*, *e*, *c*, *f*) exhibited the normal behavior of uncastrated fowls; they crowed lustily, often engaged in battle with each other and with other cockerels, and showed the usual reactions to hens. Their combs and wattles developed as in normal fowls.

Cockerel *b* was sacrificed on October 4; the remaining testis had attached itself and healed in the original site. It had increased by more than half in diameter, was richly vascularized, and showed distinct spermatic tubules; upon section a whitish fluid with many large and small cells was extruded which failed to show any spermatozoa, however.

On the same day the well developed combs and wattles were removed from cockerels *c*, *e*, and *f*, and the body cavity was opened for examination of the testis. Cockerel *e* showed the testis in the usual site, as I had also found it in the sacrificed cockerel *b*. I removed this testis from the body cavity and found it similar to that of cockerel *b*. The abdominal wound, the comb, and the wattles soon healed in this fowl, but the comb and wattles did not regenerate. The fowl began to emit the typical voice of the capon, it no longer showed interest in hens, nor would it battle with other cockerels; in fact it remained at a distance from them and showed the nature of a true capon.

In cockerels *c* and *f* no sign of the testes was observed in the usual site. Combs and wattles regenerated; the creatures retained their cockerel nature, and continued to crow and to exhibit their former behavior toward hens and other cockerels. These two roosters were killed on January 30, 1849. No sign of the testes was found in the usual site; instead in cockerel *c* it had attached itself to the ventral surface of the colon and was bordered on both sides by intestinal caeca without, however, having become attached to them. I found the same conditions in cockerel *f*, except that the testis had become attached farther caudad at about the middle of the caeca. The testis was oval in both these animals, and had a length of 15, width of 8 and thickness of 6 lines (*linien*: mm.). Well developed branches of the mesenterial arteries approached and entered the testis at various points and could be followed to the spermatic tubules. When I opened the testes, a milky white fluid exuded which had the appearance and odor of normal cockerel semen. Under the microscope I recognized in this fluid many small and large cells of 1/450 to 150 line diameter, as well as many spermatozoa with active flagellar movements, which became much more active upon the addition of a droplet of water.

These experiments yield the following results for physiology:

1. The testes belong to the transplantable organs; they may become reattached after removal from the body; actually one may transplant them from one animal to another, and the attachment may occur at the original site of removal or in an entirely foreign location, for example, on the intestinal wall.

2. The transplanted testis continues its characteristic growth as a spermatic organ even in a foreign site; the tubuli expand and enlarge and carry on normal functions in that they secrete the typical semen characterized by spermatozoa. We find here conditions comparable to those in plants where the cion retains its specific characteristics and produces its own fruit after having been grafted into the stock.

3. It is a known fact that severed nerves may be rejoined and that parts whose nerves have been cut may have sensation and movement restored after healing. But it is evident that the same fibers are not always rejoined. This may be deduced from the behavior of a restored skin transplant. From the fact that the testis may attach itself to a remote body part, namely, to the intestine, and continue to develop and actually produce semen, it follows that no specific spermatic nerves exist.* This is the chief argument against the existence of specific trophic nerves. The sympathetic nervous system has until recently been considered such a trophic system.

4. The remarkable sensuous (*consensuelle*) and antagonistic relation between the life of the individual and the life of the species, as it appears particularly at puberty and continues until advanced age, is not affected when the testes are removed from their original site and severed from their innervation and become attached to an entirely different part of the body. So far as voice, sexual urge, belligerence, and growth of combs and wattles are concerned, such birds remain true cockerels. Since, however, transplanted testes are no longer connected with their original innervation, and since, as indicated in paragraph 3, no specific secretory nerves are present, it follows that the results in question are determined by the productive function of the testes (*productive Verhältniss der Hoden*), i. e., by their action on the blood stream, and then by corresponding reaction of the blood upon the entire organism, of which, it is true, the nervous system represents a considerable part.

* Apparently the author means in a secretory sense. (Translator's note.)

AMERICAN TRUFFLES

A Thanksgiving Fantasia

HENRY E. SIGERIST

A roast turkey prepared in the good old American way with New England stuffing, and served with cranberry sauce is a great dish, but I prefer my turkey truffled and served with a sauce Périgueux. This requires some preparation but is not too difficult to make once you have mastered the elements of the art of cookery. You must buy your turkey in time. Then, two days before the event you slice some of your truffles and insert the slices delicately with your fingers between the skin and the meat of the bird without destroying the subcutaneous connective tissue altogether.

Then make the stuffing. Take some fatty tissue of the turkey, dice it and cook it with butter, chopped bacon, chopped truffles, a small chopped onion, the whole well seasoned. After it has cooked for a while, let it cool, add plenty of *foie gras*, the liver of the turkey, more chopped truffles, and fill the abdominal cavity of the bird with this mixture. And then forget about it for two days. During that period the meat exposed from all sides to a barrage of truffles, will become impregnated with their delicate flavor.

When the day finally comes, roast the turkey in the classical way, covering it in the beginning with paper that has been soaked in melted butter or olive oil. And while the bird is in the oven, make your sauce Périgueux in the following way: Cook in butter minced marinated bacon and ham, add flour, brown, add slowly rich chicken stock and a glass of good old Madeira, cook in double boiler, add minced mushrooms and truffles and at the end some of the fat from the turkey. Do not forget salt and pepper. If you happen to have a maid tell her to come after the dinner to wash the dishes, and serve the turkey yourself because meat and sauce must be served together steaming hot—which a maid never does.

This truly is a delicious dish, and I shall be glad to give a more detailed recipe to any member in good standing of the American Association of the History of Medicine who is a qualified cook. Every year I used to prepare such a turkey for the benefit of the family and of a few friends.

But now the trouble is that there are no truffles. Because truffles come from France. And because we have not yet reconquered the Périgord, the province where they are cultivated. And because if we had reconquered it, the Nazi General Staff would have eaten up the last crop anyway.

Truffles grow also in England but these truffles belong to a species that is much inferior to *Tuber melanosporum*, the best truffle of France.

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The Army Medical Library, which fortunately has a broad concept of medicine, possesses some literature on truffles, among which I found an interesting pamphlet, written by a French physician, Pennier de Longchamp fils, and published in Avignon, in 1766: *Dissertation physico-médicale sur les truffes et sur les champignons.*

The author tells us how he came to write this treatise:

> Discoveries are often made by accident and light conversation may result in useful investigations. The dissertation that I am presenting to the public owes its origin to a joke that was made during a meal about a young man who was eating a great many truffles. Since my profession obliges me to know the virtues of all the plants, I was addressed and asked what effects truffles had. I answered that the general opinion was that they were invigorating and that the gentleman finding himself in a weakened condition undoubtedly thought that he should eat many truffles in order to restore his powers. The meal was hardly over when I made it my first business to analyze them.

We can well imagine what the situation was. Avignon at that time was the same provincial and gossipy town that it is today, with old houses and narrow streets, with people who have a keen sense of humor and like good spicy food and the wine that grows across the river. In the shadow of the Palace of the Popes a group of them had come together for dinner. A dish was served, hot truffles that had been sprinkled with brandy, wrapped in bacon and in two layers of paper, the first soaked in oil, the second in water, and then roasted in hot ashes. A young man fell to and devoured them gluttonously whereupon the whole company began to kid him, wondering how he had spent the last night. The doctor should know, and they all looked at him. Dressed in black as became a man of his profession, with a jabot of lace and a wig, he tried to look serious but confirmed the general suspicion. And then it suddenly occurred to him that while he liked truffles like everybody else, he knew very little about them, and he decided to find out more.

Actually he did very little himself. He tells us quite candidly that the

analysis was made by a friend. His own major effort was to look up the literature. If anybody should have information about truffles it certainly would be a member of the Academy of Sciences, and indeed, in the *Mémoires de l'Académie Royale des Sciences* he found a paper, *Observations sur la végétation des truffes* that had been presented on February 25, 1711 by Monsieur Geoffroy le Jeune. Claude-Joseph Geoffroy (1685-1752), a pharmacist by profession, was remembered as having been an excellent chemist and botanist, and the author felt that the best he could do was to paraphrase his paper adding a remark here and there, which he actually did.

Since the truffle is a subterraneous fungus, it therefore was very puzzling to 18th century naturalists. They agreed that it must be a plant, not an excrement of the earth as some ancients had thought, yet a plant that had neither roots, stem, leaves or flower. Truffles had appeared on French menus since the end of the 15th century and both Geoffroy le Jeune and Pennier de Longchamp were familiar with their growth, cultivation and gathering. The conditions they picture are very much the same as still exist today. They tell us that truffles grow in uncultivated, reddish soil at the foot and in the shadow of trees, particularly oaks. And indeed we know that they grow best in light and porous calcareous clay soil, in association with oaks, particularly the small evergreen oaks of Southern France.

Truffles have to be "hunted" and the three methods described by our authors are still in use today. The first, and still the most popular in France, is to hunt truffles with a pig, or better, with a sow because this is an animal that loves truffles and has a very fine nose. A well trained pig may find over twenty pounds of truffles in one day during the season. But whenever it finds a truffle which is then taken away, you must compensate the pig with a few acorns "because otherwise," Pennier de Longchamp adds, "it would not persevere in a labor that is in no way profitable."

The trouble with pigs is that they are wilful animals which, moreover, tire very rapidly. Hence dogs are also used for the purpose. They must be conditioned, while they are still puppies, by having chopped truffles added to their food. If they are well trained, they may render great services and, of course, you do not reward their efforts with acorns but with bread and cheese.

And then there is a third method that you may use when you have neither pig nor dog. In such a case you walk to the oaks where you expect truffles. You lie flat on your stomach and look at the landscape

that surrounds you. If you see a swarm of tiny flies over a given spot you may hope to find a truffle there, because these are truffle flies that have the vicious habit of laying their eggs in the fungus.

"Truffles," Pennier de Longchamp tells us, "are usually served as *entremets* and our gluttons or our Epicures eat many of them because they assume that they precipitate what has already been eaten and thus develop new appetite." Medically truffles are hot and "one must admit that this is not one of the best kinds of food neither on account of its qualities nor of its modes of preparation; and individuals of sanguine and raw temperament should not eat them, nor those who by vocation are obliged to lead a life of chastity."

As modern physicians and on the basis of many years' experience, we can safely state that a truffled turkey with sauce Périgueux does not involve any health hazards. The heat it produces it hardly more than a pleasant feeling of warmth—and it certainly does not cause satyriasis.

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Since we cannot obtain truffles from France, we obviously look to America as a source of supply. We live in a great country that produces almost everything. Why should we not have American truffles?

And indeed there was a time when there were reasons for supposing that the truffle was a native of the United States. In 1812 a famous American doctor and chemist who was even a professor at Columbia University, Samuel Latham Mitchill (1764-1831) published the following letter in his own journal, *The medical repository, comprehending original essays and intelligence relative to medicine, chemistry, natural history, agriculture, geography, and the arts; more especially as they are cultivated in America; and a review of American publications on medicine and the auxiliary branches of science.* (New York, 1812, Third hexade, vol. III, pp. 335-337):

Reasons for supposing that the Truffle is a native of the United States. In a letter from D. Mitchill, *to* Caspar W. Eddy, M. D., *dated Washington, March 31st,* 1812:

Some years ago, I received from Dr. Sibley in North Carolina, a number of roundish masses, resembling yams. They were of a pure and delicate whiteness within, and covered with a brown or blackish skin. The impression I had at that time, was, that they were the roots of a plant called Tuckahoe. But I knew not what kind of vegetable, Tuckahoe was.

On further inquiry, I learned that the substances I possessed, were not roots, or if they were, they had neither radicles, buds, stems, leaves, or blossoms. This led

me to examine them again, when I satisfied myself that they were *cryptogamous productions*, of the *Lycoperdon* family. In this state of mind, I remained until very lately, when I received another specimen, and a descriptive letter from Dr. Gray, of Jerusalem in Southampton county, Virginia. It is dated January 1st, 1812, and contains the following intelligence: "I have been withheld from answering the letter which I had the honour to receive from you some weeks ago, partly by my professional engagements, and partly with a view of collecting more information concerning the vegetable in question. In this I have been disappointed. Every person of whom I inquired concerning it, has given precisely the same account, corresponding intirely with what I knew of it. I have seen it taken out of the earth at various seasons of the year, but oftenest in the spring, when it is presumed its foliage or fructification, if it had any, would be visible. I have examined the external surface, and dissected it with a view to discover if it ever had possessed a stalk or root; presuming that I might be able to discover from the direction of the fibres of the bark, whether such things had previously existed. But upon the most minute investigation, I have never been able to discover a vestige of either. The bark is of a brownish ash-colour, sulcated, and very much resembling in appearance, the root of the Papaw-gum, a species of Nyssa. It is thin, but considerably tough.

The pulp, if it may be so called, is of a snowy whiteness; and when newly dug up, soft, and abounding in a somewhat acrid juice. In this state it is said to have been used by the Indians, as a remedy in Diarrhoea.

On being dried, it intirely loses its acrimony, and acquires a bland, farinaceous, and slightly mucilaginous taste. I have no doubt it might be made a very agreeable and nutritious article of food. Its name induces one to believe that it was used in this way by the aborigines; the word *Tuche* or *Tuchai* signifying bread in several of the dialects. I believe the Tuckahoe to class among the cryptogamia. Its being intirely subterraneous, will be a barrier to the discovery of its amours. It is my design to transplant several into my garden, next spring with a view to investigate them more fully; and more especially to discover how far they may be applicable to culinary purposes. Should it be discovered that they are capable of considerable propagation, I have no doubt, they will at some future time, be an important article of agriculture.

Hogs are extremely fond of them. They inhabit, for the most part, a light rich soil; such as is best adapted to the culture of maize. Though they are sometimes found in soils of a different quality. They are frequently seen as large as a man's head, and proportionally heavy when fresh; but lose a very great proportion of their weight by drying."—

From this history, there can be no doubt that the Tuckahoe root is one of the *under ground funguses*. It seems indeed to be a species of *Truffle*, or *esculent mushroom*. In this point of view, it becomes quite an interesting object of research. To determine this, consider the character and qualities of the European Truffle.

Lycoperdon tuber.—The figure is nearly spherical, the size of a potatoe. The external coat at first white, afterwards black, and studded with pyramidal or polyedrous tubercles: the internal substance solid and callous, of a dirty white or

pale brown colour, grained like a nutmeg, with serpentine lines; in which Micheli says, are imbedded capsules, containing seeds. In Great Britain they seldom exceed three or four ounces in weight; but in Italy and some other parts of the continent, they are said to have been found of the extraordinary weight of eight, and even fourteen pounds. They are served up for food either fresh and roasted like potatoes, or dried and sliced into ragouts.—Called in English, *Truffles*, or subterraneous puffballs, growing generally three or four inches under ground, without any visible root.

Having thus drawn the comparison between this American Truffle, and that of Europe, there is reason to believe although they belong to the same genus, there is nevertheless, a specific difference.

This difference I hope some of our enterprising botanists will soon explain, and give us every memorable particular concerning it, in an authentic and explicit form. And permit me to say, I expect much from you.

With sentiments of esteem,

I am, etc.

SAMUEL L. MITCHILL

Mitchill was certainly right when he diagnosed the vegetable in question as an underground fungus but he was unfortunately wrong when he thought that it might be a species of truffle. Tuckahoe as it is called in Algonquin, or Pachyma Cocos Fr., or Lycoperdon solidum Gron., is considered to be a fungus sclerotium that grows as a saprophyte or even parasite on pine roots several feet underground.

The *Louisville Medical News* of 1877 (4:88-89) published an article by E. Scheffer on Pachyma Cocos or Tuckahoe, Hickory Pone, Indian Pone, Indian Bread, which begins:

To Prof. L. P. Yandell, jr., I am indebted for a specimen of this fungus, which he obtained from Dr. Kendrick, of Mississippi. The latter says, in his letter to Dr. Yandell: "As a rule, the pones are not found near the stumps or rotten wood, and are seldom found in old land, but generally in soil that has not been under cultivation, or only for a few years. The most of them are nearly round or oval, from the size of a turkey-egg to that of a man's head. Although he has seen more than a hundred, he does not remember to have seen more than two with a nucleus in it. He has never heard of its being used for any thing, except to make starch (?). He has never been able to get any animal, fowl, or insect to eat it."

The specimen, resembling in external appearance a piece of a root, was over seven inches long, and showed on transversal cut an oblong shape of respectively three and five inches diameter. The cortical part is of a brownish gray color, about one sixteenth of an inch in thickness, very rough, with longitudinal furrows and concentric, elevated rings; in several places it was contracted and constricted by deep depressions. The interior part of the fresh fungus is soft, easily to be cut with a knife, homogeneous; without any structure, and of a creamy white color.

Exposed to the air it soon begins to harden, deep cracks forming in every direction, and ultimately the substance becomes very hard and tough. In this hardened state it is almost impossible to powder it. The best way to reduce it to powder is to lay it in warm water, wherein it swells, and then to break the softened mass with a pestle.

The fungus under my observation has a nucleus in the form of a root, apparently, of a coniferous tree. This root goes lengthwise through the whole fungus, and has a diameter of about three fourths of an inch. This root is deprived of its cortical part, but the white substance of the fungus has, where it is in contact with the root, a different appearance; it has more of a fibrous texture and spongy appearance, while the main portion of the fungus has become quite hard and tough. No doubt the cortical part of this root gave in a certain state of decay the first cause to the formation of the fungus.

The author then gives a detailed chemical analysis which reveals that the fungus contains pectose, a little sugar and two acids one of which is oxalic acid, but no starch and no gum. This made it clear that the art of cookery had nothing to expect from that fungus.

My last hope was the U. S. Department of Agriculture, that great progressive scientific institution of our government. If somebody knew about American truffles they would know. I wrote and immediately received a very courteous answer for which I am much indebted to Mr. T. Swann Harding, Mr. J. A. Stevenson and Dr. E. B. Lambert. But the news was sad. I learned that none of the truffle species of economic importance had been found in the United States, although several small species did occur in California, Minnesota and New York. Quite apart from the fact that American truffles should by definition be bigger and better than European ones, it was all too obvious that those small species were not the right kind.

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If there are no American truffles of the best species, why do we not grow them? We have the soil that is needed. We have oaks or could import them. We have intelligent pigs and very clever dogs so that there is no reason why we should not develop a Périgord in America.

Yes, but there is a snag, namely, that it takes many years to develop a truffle industry so that it will be profitable. Once the soil has been prepared and acorns or seedlings of the right kind of oaks have been planted, truffles may appear after about five years, but it will be five to ten more years before the yield may become profitable and perhaps twenty-five years before it reaches its maximum. Hence the prospect of a truffle industry cannot be very attractive to our individualistic system of free enterprise. We have not such strong dynastic feelings that we would sow

for the next generation to reap Oh, we like to call ourselves John Doe 2nd, 3rd, 4th, 5th, . . . We also have a very soft spot for kings—as long as they are in Europe. As a matter of fact, there are several kings today whose crowns are tottering and who look to us as to their only support. But when it comes to investments, we like quick returns.

The production of American truffles, therefore, would have to be developed as a government project, by Washington "bureaucrats," under the auspices of the Department of Agriculture. But then—good God—the truffles thus produced would be socialized truffles. One might even call them "sovietized truffles," and it is obvious that no self-respecting Republican could eat them.

I can well imagine what the reaction to such government truffles grown at the expense of the tax-payer would be. The National Manufacturers Association and the Chamber of Commerce would issue a violent protest against such unheard-of government interference that was undermining the American way of life. The Council on Foods and Nutrition of the American Medical Association would investigate the matter and would publish a memorandum pointing out that truffles are un-American, a European racket for which there was no need in this country. They would draw attention to the fact that under our American system we had succeeded in raising the biggest and best turkeys in the world, that there was a turkey for everyone who knew how to ask for it, that bread stuffing was much preferable not only because its nutritional value was much greater than that of truffles, but because it conformed to American life. Whereupon the House of Delegates would pass a resolution with all votes against those of California—where good food has always been appreciated—condemning the use of truffles. The doctors of Indiana would even go one step further and would organize an Association of American Physicians and Surgeons the members of which would pledge themselves never to eat any truffles in whatever form they might be served.

And so I am afraid that we collectivists who simply adore regimentation and therefore like to eat our turkey truffled with sauce Périgueux will have to wait until the war is over and we again can get truffles from France. And this year we shall for once be individualists and shall prepare our Thanksgiving turkey like everybody else, in the good old American way. See Fannie Merritt Farmer, *The Boston Cooking-School Cook Book*, Seventh edition, completely revised by Wilma Lord Perkins, with new illustrations. Boston: Little, Brown and Company, 1942, p. 393: roast turkey; p. 211: New England stuffing: 12 slices bread, ½ inch thick. . . .

AN EARLY RECORD OF THE USE OF THE CADUCEUS IN AMERICA

BERNHARD WOLF WEINBERGER

In reviewing the literature on the origin of the Caduceus in America I have not been able to find any reference to its use in this country prior to its adoption on the coat of arms by the Medical Department of the Army in 1818. Here it appears in the form of the single serpent.

An earlier record seems to remain unnoticed and for that reason the illustrations and " Explanation " should prove of interest.

It apparently was first used by Josiah Flagg, Jr., in an advertisement that appeared in the (Boston) *Columbian Centinel*, May 26, 1792. (Fig. 1.) Later Flagg combined it with two other symbols, using the three on at least two of his hand-bills. The significance of the two dental instruments and crossed tooth brushes with the Caduceus has brought forth many conjectures and it was only recently that Flagg's intent has come to light.

Fig. 2 is a copy of the hand-bill of 1795, none of which seem to have survived the years, as reprinted on the outer cover of the *Massachusetts Magazine or Monthly Museum*. Because of the practice of removing the heavy outer covers when binding the magazine, those files examined do not contain the advertisement. Fortunately someone thought so highly of it that he had it removed and pasted in a copy of the 1793 *Low's Astronomical Diary or Almanack*, thus preserving it for a future day. We now have it in the Library of the New York Academy of Medicine.

The double entwined serpent of Mercury wound around a staff is more than of passing interest. Flagg desired, by incorporating it in the notice, to suggest that he was practicing a branch of medicine and apparently he was successful in this respect, for he continued to make use of the Caduceus throughout his professional career. He appears to have been one of the earliest in this country to utilize this symbol.

Flagg's " Explanation " and the 1795 hand-bill itself are revealing, showing a concept of dentistry hardly expected from one so early in this country. A comparison of the drawing as shown in Fig. 1 shows a slight modification, while in the hand-bill of 1796 the crossed tooth brushes were reversed.

EXPLANATION

of the Caducies (Mercury's simbol of peace), which he arrogates as Surgeon's arms. The healing art, winged with a speedy cure, and encompassed with the rays of light, knowledge or experience.

The Field *azure* is charged with a Caducies *argent*, encircled with the rays of light—Or—The Dental types on the dexter chief are two brushes, which refer to cleanliness, and the instruments in the sinister are emblematical of that last resort or cure, for the anguish which is occasioned by imprudent neglect or obstinate resistance to dental remedy.

Fig. 1. Josiah Flagg's first use of the Caduceus in the *Columbian Centinel*, May 26, 1792.

Associating the "symbol" of medicine with the importance of cleanliness of the mouth shows that Flagg must have realized some direct connection between a clean mouth and disease; this we further learn when he states: "All who may require his assistance . . . are at liberty to bring their physician and surgeon with them." The instruments themselves, he states, are the sinister warning of the last resort or cure of imprudent neglect. Here we find the forerunner of our modern scare medical advertising such as "four out of five" will have it, if?

DR. FLAGG,

Continues his PRACTICE, *as* SURGEON DENTIST *the moſt ſucceſsful of the profeſſion, in all its branches,*

FOR the extracting of the firſt teeth in children, and the regular arrangement of the ſecond ſett; for the preſerving, drawing, mending, curing, making or tranſplanting of teeth, for the adult. All who may require his aſſiſtance, and wiſh a confidence in him, are at liberty to bring their phyſician or ſurgeon with them, as he is emulous of giving perfect ſatisfaction.

He confidently aſſerts, that the ſenſation, or nerves of the teeth in the head, can be *extracted*, by a ſimple, ſafe and eaſy proceſs, with inſtruments, and the teeth ſtill preſerved and prevented from a further decay. On the truth of what he aſſerts in this, or his hand-bill he riſques his profeſſional reputation.

☞ Caſh is given for ſound live Teeth, at his Room, near the corner of *Winter-Street, two doors from Fauſt's Statue, Marlborough Street.*

EXPLANATION

of the Caducies, (Mercury's ſimbol of peace) which he arrogates as Surgeon's arms. The healing art, winged with ſpeedy cure, and encompaſſed with the rays of light, knowledge or experience.

The Field *azure* is charged with a Caducies *argent*, encircled with the rays of light—Or—The Dental types on the dexter chief are two bruſhes, which refer to cleanlineſs and the inſtruments in the ſiniſter are emblematical of the laſt reſort or cure, for the anguiſh which is occaſioned by imprudent neglect or obſtinate reſiſtance to dental remedy.

Fig. 2. [illegible] Dr. Flagg, jr., showing what is probably the earliest use of the Caducens in this country. Associated with it are two other symbols, their purpose being described under "Explanation."

The wording of the hand-bill conforms exactly with the advertisement as found in *The Federal Orrery* (Boston) November 30, 1795, therefore it must have been printed during that week, for the advertisement of the previous week reads entirely different.

These documents graphically portray just what constituted the practice of dentistry at that time. Besides the general run of duties, Flagg shows an interest in orthodontia, in oral surgery, " the sewing of hare-lips " and the " use of gold obturators," also gold dentures and inserting gold fillings.

Josiah Flagg, Jr., the son of Lt. Col. Josiah Flagg, was baptized in Boston on July 24, 1763 and lived but 53 years, dying on September 30, 1816, in Charleston, S. C., as a result of yellow fever. Little of his early life is known and it is doubtful if he served with the American forces during the Revolution as stated, for he was but thirteen when it began. History relates that he received his dental training from a French dentist who came over with Lafayette, by the name of Le Maire, and was at Newport in 1781. This story I showed (Jean Pierre Le Mayeur in America—No Longer the Man of Mystery, *Dental Cosmos*, 1934, p. 578) could not have been possible. It is more likely that he received his first dental training from Paul Revere, but there is nothing to confirm this, except that the Senior Flagg and Revere were co-publishers of songs as early as 1765.

Flagg began his dental practice in Boston before 1783, thus being one of the earliest known native-born practitioners, and continued with great success until 1812 when he enlisted in the naval service, only to be captured thereafter by the British and taken to England as a prisoner of war. While on parole during the years 1813-1815, he continued in London the practice of dentistry, being closely associated with Joseph Fox, a pupil of John Hunter and Sir Astley Cooper.

A BIBLIOGRAPHICAL NOTE ON STERNBERG

JEROME M. SCHNECK

George Miller Sternberg (1838-1915), a former Surgeon-General of the United States Army (1893-1902) and referred to by Robert Koch as the father of American bacteriology, was the author of the first American textbook of bacteriology.[1] The only biography of Sternberg ever prepared was written by his wife.[2]

Recently there has come into my possession an article by Sternberg called "Our Invisible Foes" published in 1885 in the *Journal of the Military Service Institution of the United States*.[3] It is not listed in the bibliography published in Sternberg's biography nor is it to be found in the *Index Catalogue of the Library of the Surgeon-General's Office*. This article is not in the possession of the Army Medical Library;[4] consequently it should be of some interest.

Major George M. Sternberg read his paper at a meeting of the Military Service Institution on January 8, 1885. He indicated to this military group that "well equipped armies led by able generals" have been defeated by the invisible foes more than by results of assaults of opposing armed troops on the field of battle. These invisible foes being "disease germs," he stated his intentions as follows: "The object of the present paper is to give a brief account of what is known in regard to the nature, form and *modus operandi* of these microscopic enemies of the human race, together with some information, based upon experimental data, relating to the best means of destroying them."

Sternberg went on to describe the minute size of the organisms, their methods of reproduction by simple binary fission and spore formation and the resistance of spores to temperature changes and chemical reagents. He mentioned the morphological identity of various species of bacteria

[1] Sternberg, George M.: *Textbook of Bacteriology*, New York: W. Wood and Co., 1896.

[2] Sternberg, Martha L.: *George Miller Sternberg*, American Medical Association, 1920.

[3] Sternberg, George M.: "Our Invisible Foes," *Journal of The Military Service Institution of the United States*, vol. VI, no. XXI, pp. 27-36 (March, 1885).

[4] Communication to the author from the Army Medical Library, May 30, 1944.

and their differentiation on a physiological basis. The concept of the usefulness of some species was discussed and the point stressed that " the bacteria as a class are not to be considered the ' invisible foes ' of mankind." He referred to the useful function of bacteria in decomposing organic material and their parasitic role in the determination of disease.

Dealing with the generalization that all infectious diseases are parasitic diseases, Sternberg wrote: " This generalization is not justified, however, by the present state of knowledge, and it must be admitted that satisfactory experimental evidence of its truth is still wanting in a majority of the infectious diseases which are most fatal to the human race—e. g., smallpox, scarlet fever, yellow fever, typhoid fever." He scarcely doubted the causal relation of the comma bacillus or spirillum of Koch to cholera and the *micrococcus diphtheriticus* of Oertel to diphtheria. He referred to experimental work in relapsing fever, erysipelas and anthrax and discussed the mechanical, physiological and toxic effects of bacteria in the causation of disease.

Because of Sternberg's extensive studies of yellow fever and malaria, it is of interest to read his remarks as follows: " It is possible that other more deadly disease poisons are produced . . . by the action of specific micro-organisms upon organic matter external to the human body, and that in such diseases as yellow fever and the various forms of malarial fever this is the true explanation of the *modus operandi* of the germ. However this may be we have ample evidence that decomposing organic matter, and especially that of animal origin, furnishes a suitable nidus for the external multiplication of the germs of yellow fever, of cholera, and of typhoid."

In discussing disinfection he stressed the importance and effectiveness of fresh air ventilation of sick-rooms and mentioned as unreliable disinfectants, sulphate of iron, sulphate of zinc, chloride of zinc, and carbolic acid. He stated that he was engaged in experimental work on disinfection and advocated the use of sulphur dioxide for disinfecting ships, hospitals and dwellings. A one to one thousand solution of bichloride of mercury was suggested for disinfecting clothing and a one to five hundred solution for use on sputum and feces. For the latter purpose the use of Labarraque's solution (liquor sodae chlorinata) was also advised.

Sternberg's article consumed ten pages of the journal in which it was published. This issue contained in addition an article on " The Militia "

by General William T. Sherman, an article on "Camp and Garrison Sanitation" by General Egbert L. Viele, correspondence, association reports and book reviews including a discussion of *Bacteria* by Drs. Antoine Magnin and George M. Sternberg.[5]

[5] Magnin, A. and Sternberg, G. M.: *Bacteria*, New York: W. Wood and Co., 1884.

UNIV. OF MICH.

Frans Cornelis Donders (1818-89) in middle and later life.

CARSON, LUDWIG, AND DONDERS AND THE NEGATIVE INTERPLEURAL PRESSURE

N. S. R. MALUF

One's attention is drawn by the striking fact that Carl Ludwig (1816-95), who was the first to insert a cannula into the interpleural cleft and thus record the respiratory fluctuations in interpleural pressure (1847)—the first direct observations on the interpleural pressure—, did not actually state that the pressure is negative or subatmospheric. He was doubtless aware that the pressure must be negative because he noted pneumothorax and tried to mitigate the damping effects of partial pneumothorax upon his kymographic tracings by attaching a thin-walled rubber balloon to the end of the cannula which was to be inserted and filling the balloon and cannula with water. The genius from Marburg must have realised that the negative interpleural pressure *per se* is of no physiological significance and was therefore not worth mentioning. His paper dealt with the effects of the respiratory movements on arterial pressure. It can be shown by the simple laws of hydrostatics that only *fluctuations* in interpleural pressure can be of circulatory importance and not negative pressure as such. This remark applies especially to the venous return but its treatment is outside the scope of this note. Ludwig recorded merely what is important—the *fluctuations* in interpleural pressure—and did not compare interpleural pressures with atmospheric pressure.

The interpleural (or, less accurately, intrapleural) pressure is sometimes called " Donders' pressure " because Frans Cornelis Donders (1818-89), physiologist, ophthalmologist, and pathologist of Utrecht, first enunciated, in 1853, that it is negative. He pointed out that it is negative because of the retractile tension of the lung. He measured the pressure produced by the recoil of the lungs and was the first to state that the interpleural pressure must be less than atmospheric by an amount equal to the positive pressure produced by the recoiling lung. This indirect method of measuring the interpleural pressure had been used by James Carson (1772-1843) of Liverpool who described it in 1820. Carson, however, merely wanted to measure the pressure produced by the recoil of the lungs and did not state its implications with regard to a negative interpleural pressure. Donders mentioned Ludwig but not Carson in his paper. I do not think it correct to say that Donders actually discovered the negative interpleural pressure. Donders merely stated a

Frans Cornelis Donders (1818-89) in middle and later life.

physical fact without introducing any essentially new data to bear directly on the matter. Moreover, Ludwig had already made direct observations on the interpleural pressure although he did not explicitly say that the pressures are negative.

It is difficult to find a single source for the commonly seen statement that the negative interpleural pressure is a determining agent in keeping the lungs expanded in the (normal) chest. Carson, Ludwig, and Donders made no such claim—Ludwig (1847) evidently did not think a negative interpleural pressure, as such, worth discussing. Michael Foster's textbook has the error. Shall we consider his book, at least as far as we are concerned, as representing "the year One?"

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MEDICO-HISTORICAL NEWS AND ACTIVITIES

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE

CONSTITUENT SOCIETIES

New York Society for Medical History, New York

A joint meeting of the New York Society for Medical History and the Section on Historical and Cultural Medicine of the New York Academy of Medicine was held on November 8, 1944 at the New York Academy of Medicine. The topic of the evening was "Medical Libraries and Medical History" with Miss Gertrude L. Annan, Dr. Walton B. McDaniel, 2d, and Dr. Bernhard W. Weinberger as the speakers. Miss Helen Bayne, Mrs. Josephine G. Nichols, Mr. Seymour Robb, and Mr. Frank Place participated in the discussion.

NATIONAL NEWS

Michigan

Last year we reported that the "Early House" on Mackinac Island where Dr. William Beaumont treated Alexis St. Martin had been turned over to public ownership as a Beaumont memorial (*cf.* this *Bulletin*, Vol. 14, pp. 526-527). At a recent ceremony, Mr. Wilfred F. Doyle, chairman and resident commissioner of the Mackinac Island State Park Commission, presented a gavel carved from a piece of wood from the "Early House" to the Council of the Michigan State Medical Society. The gavel is composed of white pine wood which was grown on the island.

NEWS FROM LATIN AMERICA

Ecuador

The Universidad Central de Quito has just created a chair of the History of Medicine with Dr. Virgilio Paredes Borja as Profesor Titular. This new chair and the growing list of publications on medical history from our South American neighbors testify to their ever increasing interest in the subject.

Mexico

A ceremony in honor of Dr. William Harvey was held in the Department of Physiology of the Facultad de Medicina de la Universidad Nacional Autónoma de México on October 30, 1944. The program, at which Dr. Alfonso Caso, Rector of the University, presided, included the presentation of a bronze bust of Harvey executed by Dr. J. G. Martín del Campo, an address by the English ambassador, Mr. Charles H. Bateman, and a paper on "Harvey's Place in the History of the Scientific Method in Biology" by Dr. J. J. Izquierdo, the Head of the Department of Physiology.

Peru

The *Anales de la Sociedad Peruana de Historia de la Medicina*, Vol. VI, Año 1944 has just been received. The volume contains the following articles:

El Cuatricentenario de la "Fábrica" de Andreas Vesalius, y las bases anatómicas de la Escuela Médica de Lima. Dr. Carlos E. Paz Soldán.

El médico de Almagro. Dr. Juan B. Lastres.

La Medicina árabe y su influencia en Occidente. Dr. T. Majluf.

El Renacimiento anatómico. Dr. Julio Faldini.

"Locos de la Colonia." Dr. Carlos Martínez Durán.

El interesante cráneo de las "chullpas" de Sinsicap. Dr. Lizardo Vélez López.

Discurso del Presidente de la Sociedad, doctor Carlos E. Paz Soldán, en la solemne Sesión de Aniversario.

Precedentes en la historia de la Medicina Peruana. Discurso del Dr. Manuel A. Pulido Méndéz, Embajador de Venezuela.

Emile Sergent, elogio pronunciado por el Dr. Juan B. Lastres, el día 20 de julio de 1943.

NEWS FROM EUROPE

Switzerland

The 124th Annual Meeting of the *Schweizerische Naturforschende Gesellschaft* was held this year from September 2 to 4 at Segl/Sils im Engadin. The meeting included a section of the History of Medicine and Science.

ERRATUM

The Editors wish to point out an erroneous date occurring in Essays in the History of Medicine Presented to Professor Arturo Castiglioni on the Occasion of His Seventieth Birthday April 10, 1944 (*Supplements to the Bulletin of the History of Medicine*, No. 3) which was overlooked in proof-reading. On page 114, at the end of the second paragraph, the date of Benjamin Morris' death is given as May 14, 1750. It should read May 14, 1755.

BOOK REVIEWS

ARISTIDES A. MOLL. *Aesculapius in Latin America.* Philadelphia and London: W. B. Saunders Company, 1944. 639 pp. 179 ill. $7.00.

This is the first systematic history of medicine in Latin America, and a very satisfactory one too. The author, secretary-editor of the Pan American Sanitary Bureau, Washington, former editor of the Spanish Edition of the Journal of the A. M. A., former secretary of Pan American Sanitary Conferences, etc., was well prepared for a task which is full of extreme difficulties. The author devotes about equal parts of his book to the colonial period (1492-1808) and the period of independence. Even a very short resumé of this history which covers an enormous field in time and space is impossible in this context. Therefore we can give here but a few general comments.

The medical history of Latin America emphasizes a fact too often overlooked by the European and the Anglo-American: that Latin America is at least as much American—historically and psychologically speaking—as it is Latin. Many of the problems of South American medical history sound very familiar to the Anglo-American: the Indian background; the role played by epidemics, especially yellow fever, in shaping medicine; priests as the first practitioners of medicine; the flowering of quackery; the fight for an adequate medical education, etc.

Latin America is 100 years older than Anglo-America and its colonial period is characterized by a more systematic form of government. Latin America, therefore, had some important institutions earlier (hospitals, universities, printing presses), and some aspects of medicine (public health, licensure, quarantine) were not only earlier but better developed. These are the positive sides of the monarchic-catholic background of Latin America which otherwise had enormous drawbacks and sometimes created an almost medieval atmosphere unknown in Anglo-America (throttling of education, division of healers into physicians, surgeons and other classes, etc.). The revolutions of the XIXth century partially removed these obstacles as for instance the color line, and the great number of outstanding South American physicians of Indian blood in the period of independence show the soundness of this policy. Latin American medicine was the melting pot of perhaps even more foreign influences (carefully described by the author) than was Anglo-American medicine. The end of the colonial period, the late XVIIIth century, saw in Latin America a flowering of medicine, characterized by the names of Espejo, Vargas, Unanue and easily the equal of the Rush, Morgan period. The colonial period of Latin American medicine as a whole is rather brilliant.

The permanent unrest in and between the South American republics, the dependent economic development and the poverty of these countries retarded considerably the evolution of Latin American medicine during the XIXth century. Latin America did not play much of an independent role in the heroic period of modern scientific medicine, while Anglo-America at least partly succeeded in doing so. It is typical that Latin America produced great clinicians during this period,

but no physiologists, pathologists, etc. Only in the XXth century does the contribution of Latin America, especially in such fields as microbiology, parasitology, bacteriology, symbolized by the names of Cruz, Chagas, Carrion, Rangel, etc., win international fame. Social security is better developed than in Anglo-America. Hostility towards the practising of medicine by women seems common to both Americas. Pan American collaboration in health questions is a reality (collaboration in health problems was also one of the brighter aspects of the late League of Nations).

The author gives two excellent chronologies (chronology of disease, and chronology of medicine) as appendices. It is probably inevitable that in a work of these proportions a number of little inaccuracies should creep in (for instance the first North American woman doctor's name was Blackwell, not Caldwell; the Peruvian medical historian Lastres did not die in 1929, but fortunately is still with us; the Chilean Machi did not actually open the body, but performed a shamanistic trick still practised by Siberian and Eskimo shamans, etc.). A work of this character also probably cannot avoid repetitions, and lists of modern physicians which are sometimes rather tiresome. It is also regrettable that a number of portraits are reproduced in a way which makes them rather caricatures.

These few critical remarks are neither intended nor able to impair the great fundamental value of the book which is not only a first attempt to fill a most lamentable gap and to satisfy an urgent need in our literature, but which in itself is a great accomplishment.

ERWIN H. ACKERKNECHT.

JAMES V. RICCI. *The Genealogy of Gynaecology. History of the Development of Gynaecology throughout the Ages, 2000 B.C.-1800 A.D.* Philadelphia, The Blakiston Co., 1943. 578 + xxi pp. Illustrated. $8.50.

As the subtitle indicates, the present volume is a history of gynecology from 2000 B.C. to 1800 A.D.; the period from 1800 to 1900 will be covered by a second volume still to come. It seems, therefore, reasonable to review the book not only for its own value but also with an eye to the promised continuation.

The need for a comprehensive history of gynecology cannot be doubted. While there exist several histories of obstetrics, the history of gynecology has as yet not been treated in the same thorough way. Isidor Fischer's *Geschichte der Gynäcologie*,[1] is hardly more than a general, though thorough, survey of the material, McKay's *History of Ancient Gynaecology*[2] ends with the Arabic writers, and Diepgen's *Die Frauenheilkunde der alten Welt*[3] is concerned only with antiquity. It is nevertheless regrettable that Dr. Ricci apparently was not cognizant of the

[1] I. Fischer. Geschichte der Gynäcologie, in: *Biologie und Pathologie des Weibes*, herausgegeben von J. Halban und L. Seitz, 1. Bd., Berlin und Wien, 1924, pp. 1-202.

[2] W. J. S. McKay. *The History of Ancient Gynaecology*, New York, 1901.

[3] Paul Diepgen. *Die Frauenheilkunde der alten Welt*. München, 1937 (Handbuch der Gynäkologie, herausgegeben von W. Stoeckel, 12. Bd., 1. Teil).

latter work. If he had been able to consult it, he would have avoided many inaccuracies.

Dr. Ricci has approached his task from a very broad point of view. He is undoubtedly right that a history of gynecology cannot be rigidly separated from the development of obstetrics. Being aware of the fact that gynecology is a part of medicine, he has not hesitated to refer to the broader framework and, in addition, to introduce every chapter with a sketch of the political and cultural development of the period under discussion. There will be few to deny the desirability of relating the history of a specialty to the forces that shape the conditions of medicine and of man's mind. However, to be successful, such a relationship must be clearly traced and pointed out. The reader is little helped by being reminded of some elementary historical facts to which very little reference is made in the strictly gynecological discussion. As they are, these introductory sections could have been left out without loss to the book.

Dr. Ricci has arranged his material in the traditional geographical and chronological order, subdividing it into the Prehistoric Period, the Ancient Epoch (Egypt, Babylonia-Assyria, Hindu and Biblical literature), the Classic Age, the Byzantine Period, the Arabic Era, the Medieval Epoch and the Transitional Period. The latter comprises the Renaissance and the seventeenth and eighteenth centuries and fills almost a half of the book. For purposes of this review we shall consider the time from the early beginnings to the end of the Middle Ages first and shall discuss the "transitional period" afterwards.

Historical work dealing with oriental cultures, Antiquity and the Middle Ages requires familiarity with philological and historical methods. Even the best knowledge of the subject matter itself, in this case gynecology, cannot replace this familiarity. As long as physicians received a classical training they were equipped to some extent with the tools necessary for such research. In our own days classical training has largely disappeared from the education of the physician, and he is no longer prepared to deal adequately with the remote part. Thus we witness the appearance of books which discuss Greek and medieval medical subjects in an inadequate manner, and unfortunately Dr. Ricci's book is no exception. It abounds in inaccuracies which go beyond any excusable amount. It is true that the chronology of the Babylonian kings is hard to establish with absolute certainty, but I do not think that any modern scholar has ever placed Hammurabi at "around 725 B. C." (p. 28). It is also true that we know little about the life of Hippocrates. But we do know that he did not learn medicine at a temple of Asclepius in Cos (p. 52), for the simple reason that no such temple existed in Cos at the time of Hippocrates. The exact relationship between the gynecological work of Soranus written in Greek and the Latin paraphrase attributed to one Muscio still poses many interesting problems. But Dr. Ricci's statement that "Soranus' original treatise was written in Latin, and it was later translated into Greek" (p. 127) as well as the rest of his account of this very important book, confuse the whole matter. On page 274, Dr. Ricci writes: "Long after the Renaissance a popular source of therapeutic knowledge was the ninth book of Rhazes' *Continens*. This treatise was annotated by Marco Gatinaria and later translated by Vesalius." This ninth book belonged, of course, to Rhazes' work "Ad Almansorem" and not to his "Con-

tinens" and had been translated long before Vesalius who wrote a paraphrase of it. These few examples taken from periods between 2000 B. C. and the sixteenth century must suffice to bear out the contention that the entire first half of the book cannot be used as a reliable guide. A truly formidable list could be made up if all the wrong data, wrong titles, and impossible quotations were brought together. It is possible that at least part of them may be due to printing errors, of which very few books are free. In the opinion of this reviewer it is trivial to point out isolated misprints. Unfortunately, in this book it is not a question of isolated misprints but of such a large number of mistakes that it is simply impossible to distinguish between the author's shortcomings and a careless handling of the manuscript.

This reviewer cannot help feeling that it would be better if such works as the present one omitted a detailed discussion of ancient and medieval times and instead confined themselves to an introductory chapter to the modern period. In the case of the present book there is even more reason for such a suggestion because a large part of the ancient material has already been covered by McKay. A short resumé with a guide to the main literature would, therefore, have been sufficient.

We now come to the second half of the work which Dr. Ricci calls the "transitional period" and in which he obviously feels more at home than in the preceding chapters. This is not to say that this half is free from the blemishes which characterize the first half. However, they become fewer in number and less obvious as the work proceeds; and, what is more important, the manner in which the material is treated changes. Whereas in the preceding chapters Dr. Ricci outlines the work of individual physicians, he now presents cross-sections through the knowledge and progress of gynecology in the seventeenth and eighteenth centuries. For these centuries the book really assumes the character of a history of gynecology. The material is presented in the form of many subdivisions such as "the anatomy of the female genitalia during the seventeenth century," "views on gonorrhoea in the female in the seventeenth century," etc. Outstanding individual contributions are given due emphasis and the whole is blended into a unit from which one can learn what was generally known and done, as well as what new ideas and discoveries originated. It is to be hoped that the author will be able to carry over this method into the promised continuation of his book and to keep the second volume free from the shortcomings of the present one.

Dr. Ricci undoubtedly has worked through a tremendous amount of material, and only great enthusiasm can have enabled him to accomplish his book. In so far as paper, printing type and illustrations are concerned, the publishers have succeeded in giving it an impressive appearance. If in the promised continuation data are checked, sources quoted correctly, misprints and impossible quotations avoided as far as humanly possible, we may look forward to a history of gynecology in the nineteenth century that will be a reliable reference work for the medical historian and a useful text for the historically interested gynecologist.

O. Temkin.

Sir William Cecil Dampier. *A Shorter History of Science.* Cambridge, at the University Press. New York: The Macmillan Company, 1944. x + 189 pp. Illustrated. $2.00.

The author of this book has attempted nothing less than to write a history of science from the origins to the present in the space of less than 200 pages. In the nature of the case the result is bound to be unsatisfactory. The story often degenerates into an annalistic cataloguing of names and discoveries; and the excessive brevity produces its inevitable crop of half-truths and confusions.

The fact is that Sir William's earlier book, *A History of Science and its Relations with Philosophy and Religion* (Cambridge, 1929) is one of the best works in the field. One can only conclude that he was badly advised to produce what the jacket of the new book so revealingly calls "a streamlined storehouse of information."

This is not to say that short books in this field are not to be welcomed. Editions and translations of the classics of science (cf. *Bulletin of the History of Medicine*, June, 1944, pp. 1-12) and biographies of the great scientists would be most useful for the types of reader that Sir William is seeking to reach. But in my opinion these readers will neither be inspired nor significantly instructed by this Shorter History of Science.

I. E. Drabkin.

Leon B. Richardson. *Fifty Years of Service: A History of the Mary Hitchcock Memorial Hospital.* Hanover, N. H., 1943. 80 pp., illustrated.

Jane Benedict, Compiler. *The Story of the First Fifty Years of the Mount Sinai Hospital 1852-1902.* New York: The Mount Sinai Hospital, 1944. 92 pp., illustrated.

In lieu of an elaborate celebration of its 50th anniversary because of wartime conditions, a brief history of the Mary Hitchcock Memorial Hospital in Hanover, New Hampshire, has been prepared by Mr. Leon B. Richardson, one of its Trustees. Hiram Hitchcock, the founder, was a wealthy New York business man who purchased an estate in Hanover when he retired in 1870. Being interested in community affairs, his attention was drawn to the lack of adequate hospital facilities in the region, and he therefore decided to erect a hospital in memory of his first wife, Mary Maynard Hitchcock who died in 1887. The building, also designed to serve the Dartmouth Medical School, was erected in 1893 entirely at Mr. Hitchcock's expense and followed the most advanced views of the day on hospital construction. Its original capacity of thirty-six beds has been increased through a continual enlargement of the plant, until today it accommodates 196 and is the largest general hospital in New Hampshire.

The problems of finance and expansion occupy the greater part of Mr. Richardson's history. Presented to the community in 1893 without any endowment, for Mr. Hitchcock met financial reverses soon thereafter, the hospital has successfully grown through the gifts of patrons and the support of the people in Hanover and

the surrounding towns. From the beginning the majority of the beds were intended for paying patients, with the exception of the "free beds," i. e. those endowed and occupied without charge by patients whom the donor had the privilege of choosing. Such free beds were frequently endowed by neighboring towns.

In 1927 the professional staff of the hospital organized themselves into the Hitchcock Clinic, the first group clinic in New England. Recognizing the greater advantages derived from group practice and the more economic and competent method of examining and treating their patients, the individual physicians gave up their private practices. The Clinic was so successful, with patients coming to it from all over the country, that it created the need for the most recent enlargement of the hospital, that made in 1938.

* * *

While Mr. Henderson's booklet discusses an institution that is only fifty years old and therefore falls within the realm of very recent history, thereby excluding an extensive treatment of personalities and medical procedures, *The Story of the First Fifty Years of the Mount Sinai Hospital, 1852-1902* takes one back to mid-nineteenth century New York City and the medical constellations of that day. Miss Benedict has very successfully pictured the origin and growth of Mt. Sinai within the larger framework of the other historical events contemporaneous with it: the growth of New York City, the leading physicians, the type of medicine which was practised, the introduction of new techniques, etc. The reader is thus granted a well-rounded description with complete documentation.

Mt. Sinai, the first Jewish hospital in the United States, originated as a charitable institution to provide medical care for the needy, and throughout its existence this has been its chief function. Its staff has included many eminent physicians of New York such as Valentine Mott, Willard Parker, Abraham Jacobi, Mary Putnam Jacobi, Thomas Markoe, Paul F. Mundé, Emil Noeggerath, Emil Gruening, Arpad G. Gerster, Edward G. Janeway, Bernard Sachs and Emanuel Libman. Financed entirely by private donations and subscriptions, in the period under discussion the hospital outgrew two buildings and kept pace with the increasing demands made upon it, treating yearly 88 to 96 per cent of its patients free of charge. When modern scientific medicine with its X-ray and extensive bacteriological and bio-chemical procedures appeared at the end of the last century, Mt. Sinai soon provided the necessary equipment and personnel. From a mere "home of the sick" it became an institution capable of advancing beyond its initial function to that of furthering medical science.

We are told that the most recent history of Mt. Sinai Hospital from 1902 to the present is now in preparation and will be published in the *Journal of the Mount Sinai Hospital.*

GENEVIEVE MILLER.

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